Genetic Services: Developing Guidelines for the Public's Health

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TABLE OF CONTENTS

Preface

Genetic services improve the health of individuals, families, and populations through the detection of inherited environmental sensitivities with appropriate intervention to maintain optimum health. We traditionally have realized this powerful paradigm in state public health newborn screening programs where diagnosis and intervention for diseases such as phenylketonuria (PKU) and galactosemia save thousands of children each year from death or mental retardation. The Council of Regional Networks for Genetic Services (CORN) recognized the potential harm of early post-partum hospital discharge as a national issue, convened a conference and published our national experience in the monograph, "Early Hospital Discharge: Impact on Newborn Screening" in 1995.

This year, CORN broadens the definition of "genetic services" and is developing a guidelines framework for genetic services as applied to the public's health. CORN's goal is to improve genetic service delivery, and consequently, the quality of life for those with rare and common heritable disorders alike. Our first objective is to encourage and document communication among the interrelated genetics organizations including consumers; laboratory and clinical medical geneticists and counselors; state, regional, and federal public health providers; and human genome investigators whose efforts hold promise for expanding our knowledge of heritable causes of disease and may yield the benefits of public health-based genetic services which prevent them.

This conference addresses these interdependent relationships in seven parts. Part One highlights the efforts to define guidelines for services at a national, regional, and state level. Part Two compiles the experience of professional medical genetics organizations in developing guidelines and refers to published guidelines in managing specific heritable disorders. Part Three addresses the changing dynamics in financing genetic services, including the impact of national legislation and managed care on service delivery. Publishing guidelines for genetic services poses difficult ethical and legal questions which we probe in Part Four and consider recommended courses of action. Part Five explores guidelines for present and future use of laboratory-based genetic screening. One of the most important services provided by geneticists is public and professional education. Therefore, in Part Six we develop definitions of education as a genetic service and outline available national educational resources. We acknowledge the importance of cultural relevancy in education and consider the issue of public health directiveness versus nondirective genetic counseling. Part Seven anchors the conference in the dynamic field of genetic research and offers us a glimpse of what public health services may emerge when researchers fully sequence the human genome. This finale reminds us that guidelines are, and should remain, mutable as knowledge about genetics and its impact progresses.

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The Human Genome Project: A Challenge to Public Health

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On behalf of the Maternal and Child Health Bureau of the Health Resources and Services Administration, I would like to extend a warm welcome to you all to this important conference. I want to express my personal appreciation to Dr. Skip Elsas, CORN President, and members of the CORN Planning Committee for their insight in selecting this timely topic for the conference, and for their effort in bringing together an excellent faculty to address the diverse aspects of developing guidelines for genetic services in public health programs.

Genetic services are not new to public health programs. In fact one of the most cost-effective public health programs, screening newborns for PKU and other metabolic disorders, came into existence more than three decades ago in the 1960s. In the early 1970s, sickle cell anemia gained wide public attention, not all of which was appropriate or beneficial to the population served. Those well-intentioned but poorly conceived sickle cell programs left behind many painful lessons about the potential dangers of providing genetic services improperly such as employment and insurance discrimination. Although newborn screening and sickle cell programs have continued to be important public health programs, other types of genetic services have received little public attention and funding. Today, genetic services remain among the most poorly funded public health programs. Perhaps a major reason for this neglect is the general perception that genetic disorders are relatively rare and are, therefore, of little reference to public health programs which have traditionally been concerned with diseases of high prevalence and epidemics. Moreover, public health programs have relied heavily on highly effective intervention strategies, but for most genetic disorders, interventions are still quite limited today.

But we have now entered into an era in which the Human Genome Project has begun to uncover a role for our genes in virtually every type of diseases. We can no longer think only of the relatively rare single gene disorders in planning for genetic services. We must also consider a long list of conditions ranging from metabolic disorders, cardiovascular disease, hematological disorders, cancer, and neuropsychiatric disorders to susceptibility to infections and other environmental insults. Deeply troubling is the fact that what we know today about the role of genetic factors in human health and diseases is only the tip of the iceberg, compared to what we will know in five to ten years as the Human Genome Project marches toward its completion. Who will translate these exciting research findings into services that actually benefit the human race?

Today, to truly serve the public well, public health programs must plan to cope with the explosion of scientific knowledge and technology in genetics that has already begun. Conversely, the genetics research community which is responsible for these scientific advances must look to public health programs to help to translate these advances into human services. It is precisely because of this

inevitable inter-dependent relationship between these two unlikely partners that CORN has, and should continue, to play a pivotal role in fostering a close and enduring partnership between the genetics and public health communities, and guide the future of genetic services. And for this important task, we need a set of guidelines.

As we proceed, many challenges lie ahead, and I will mention only a few. First, the highly prescriptive approach used by public health programs, often involving legislative mandates, is diametrically opposite to the central tenet of non-directiveness in genetic counseling. How should this critical difference be reconciled? Is it time for the genetics community to re-examine the tenet of non-directiveness and define its limitation in applicability? Should recommendations be made, for example, when presymptomatic detection and intervention are clearly beneficial? For public health programs, their heretofore unequivocal emphasis on primary prevention can become a serious problem when applied to reproductive genetics, because of the danger of eugenics and the need to respect the rights of the disabled. Where legislation mandates exist, such as in newborn screening, what is the appropriate approach to informed consent and personal autonomy in genetic testing? When is the non-directive approach appropriate in public health programs? How will access to genetic services in public health programs be assured under managed care, which has expanded its role in both public and private health services? What should we do about insurance, employment and other discrimination based on genetic information?

These are but a few of the challenges that confront us as we prepare to develop guidelines for genetic services for the public's health. I hope that with careful consideration of these challenges and other issues, at the end of the conference, the panels together will provide CORN and the Maternal and Child Health Bureau with a clear road map for the future of genetic services in public health programs.

Opening Remarks

A.H. Nora. Assistant Surgeon General, Director, Maternal and Child Health Bureau, Health Resources and Services Administration, Rockville, Maryland

It is a pleasure for me to talk to you this morning at this conference on developing genetic service guidelines for the public's health. First, however, I want to compliment you on last year's symposium where you addressed the issue of early hospital discharge, which is becoming an increasing problem. The proceedings published from that conference have been an excellent resource in examining this critical issue for our nation's mothers and infants. Currently, five states have enacted legislation concerning length of hospital stay for childbirth, 22 states have had legislation introduced, and 4 states are expected to take some legislative action in the near future. The Health Resources and Services Administration (HRSA) is deeply concerned about the consequences of early discharge, and is committed to going beyond the anecdotes to determine exactly what impact the practice is having on babies and mothers. As hospital stays for childbirth have decreased, (from 3.9 days in 1970 to 2.1 in 1992 for vaginal deliveries), HRSA has taken the lead in assessing the trend. Since 1994, HRSA has convened expert panels and commissioned three reports to determine what science says on the issues. Last September, the Maternal and Child Health Bureau (MCHB) awarded a grant to the University of California at San Francisco to operate a coordinating center for research on early discharge. HRSA is also planning an early discharge summit for April to strategically plan on how to assure that mothers and children get appropriate and quality care.

The Bureau's role in developing genetic services in public health programs has been long-standing. For more than 30 years, we have supported efforts to develop genetic service programs nationwide. It is clear that these programs have been successful because of partnerships such as the one MCHB has with the Council of Regional Networks for Genetic Services (CORN).

CORN has played a key role in integrating genetic services into public health programs, specifically into maternal and child health programs, performance partnerships, and quality assurance outcome measures. To improve genetic services in these programs, national guidelines must be developed.

Over the last several years, many of the regional networks have developed guidelines for their own use. However, national guidelines will play an important role in assuring the quality of genetic services in the future. There are many factors that will guide and influence the development of genetic service guidelines for the public's health and will determine our ability to serve the nation's mothers and children.

As many of you already know, the federal government is operating under a continuing resolution until March 15, 1996. Presently, the Bureau is operating at 45% of $683,950,000. After the 15th, we are not sure what will happen. However, it is possible that another continuing resolution will be signed by the President and the Bureau would then operate under the level prescribed into law, so in the coming months we need to watch carefully and wait to see what happens.

One of our biggest challenges in these times of reduced financial resources is to guarantee that we don't lose sight of our mission and the populations we serve. We must convince the Congress that what we are doing is essential and we must spread existing resources as broadly and evenly as possible.

Public health programs will be increasingly involved with genetic services because of the explosion of scientific knowledge and technology associated with the Human Genome project. It is imperative that federal leadership identify areas of need and provide guidance and seed money, to develop new services and fill in the gaps.

CORN: Guidelines for Clinical Genetic Services for the Public's Health

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New developments in human and molecular genetics are certain to have an impact on the majority of families in the United States, irrespective of ethnic, cultural, or socioeconomic background. Few families are without an incidence of, for example, cardiovascular disease, cancer, diabetes, or mental illness among older generations, pregnancy loss, birth defects, and developmental delays in the younger ones.

Service resources, however, are dwindling, medical practice patterns are changing, and progressively less professional time is available for supportive communication and the provision of information to patients/families about issues specifically relevant to them.

These changes have resulted in the recognition by the Maternal and Child Health Bureau, the genetics professional community, and the general public of the need for stability in the provision of genetics services within the state and territory public health agencies. The draft of the guidelines for genetics services presented here are being prepared as a resource for public health agencies as these agencies assess the needs within their own states/territories for all types of genetics services and as they facilitate the accessibility and availability of these services.

Bearing in mind that each state/territory has different geographical, ethnocultural, demographic, and other needs, these guidelines are intended as a true framework.

The first part of the framework is a suggested organizational/administrative structure consisting of a state/territory "genetics coordinator" and an advisory council who together design a state plan. This is followed by a list of potential types of family, population, and laboratory services.

It is understood that not all facilities (clinical, laboratory, etc.) can be available in every state or territory. The framework indicates those that should be available on a regional, even national basis to families or populations who need them occasionally.

Strong emphasis is placed upon the preventive potential of genetics services because, apart from the benefits of newborn screening, little is known about the contribution of medical genetics to the prevention of many common disorders. Formal qualifications of genetics staff, facilities for clinics, the need for privacy, confidentiality, ethical/legal issues are included, as are the needs for accurate documentation of genetics services and sources of funding unique to every state and territory.

These evolving guidelines are presented for consideration and adaptation to the needs of each state or territory. As mentioned previously, they represent a basic framework. In other words, they are not meant to provide guidance about the practice of medical or clinical genetics. Several types of specific practice guidelines are currently also being developed by members and committees of the

American College of Medical Genetics, the American Board of Genetic Counseling, and others, which address management protocols for individual disorders or groups of disorders, such as Down syndrome, mental retardation, stillbirths, breast cancer testing and counseling, the approach to the dysmorphic child, and others. Examples of some of these are also presented in this publication and were reported upon at the conference on Developing Guidelines for the Public's Health.

For the several states/territories who are in the process of developing their own specific guidelines for genetics services, the framework presented here should provide an additional source of information. The ultimate goal is common to all of us. It is to reduce mortality and morbidity and to alleviate suffering associated with genetic/congenital disorders. It is to help patients and families understand and cope with their own specific genetic disease or risk thereof within the context of their own psychosocial, cultural, and ethnic background.

GUIDELINES FOR CLINICAL GENETIC SERVICES

FOR THE

PUBLIC'S HEALTH

(DRAFT)

Council of Regional Networks for Genetic Services

June, 1996

PLEASE NOTE: This is a working document; not to be taken as final.

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GUIDELINES FOR CLINICAL GENETIC SERVICES FOR THE PUBLIC'S HEALTH

Purpose

The purpose of this document is to provide state and territorial public health agencies with an outline of suggested components for a genetic services system. Individual states and territories vary considerably in their genetic service needs. Therefore, this document has been designed to be used as a guideline by local communities and agencies in developing their own comprehensive genetics plan.

Public health agencies are responsible for: 1) collecting and analyzing data to identify problems and community needs; 2) setting health goals, and identifying and mobilizing the resources to achieve these goals; and, 3) assuring quality and access to services to those in need of these services. This document serves as a resource tool for background on genetics and public health implications, data collection, and funding sources. The document emphasizes service delivery with descriptive backgrounds of types of genetic services, personnel, and quality assurance references.

Genetics is a rapidly developing discipline which is providing us with the knowledge to: 1) prevent the occurrence of many birth defects; 2) treat the sequelae of genetic disorders; and, 3) decrease the burden of chronically disabling diseases such as cancers, diabetes, and heart disease. While the lives and health of thousands of newborns have been saved by successful population based screening for inherited metabolic disorders, the many other ways in which genetic services preserve health and prevent suffering have yet to enter the domain of public health (1) and the awareness of primary care providers.

The ultimate goal of genetic services is to reduce mortality and morbidity, and to alleviate suffering associated with genetic/congenital disorders. These services exist to help patients and families understand their specific genetic disease or risk thereof within the context of their own psychosocial, ethnocultural background.

It may be unrealistic to expect every state or territory to develop a complete system of genetic services. Health care delivery is changing rapidly, particularly in the rise of for-profit service delivery and managed care organizations. Public health agencies will play a critical role in overseeing these changes and assuring access to quality genetics care for their populations. The Council of Regional Networks for Genetic Services (CORN) recommends that each state/territorial public health agency become acquainted with its own Regional Genetics Network as well as with CORN. These networks are resources for each state or territorial public health agency (Appendix A).

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BACKGROUND INFORMATION FOR GENETIC SERVICES AND THE PUBLIC HEALTH

I. The Changing Face of Human Disease

Health care during the first two-thirds of the 20th century was characterized by a significant reduction in the occurrence of infectious diseases around the world. Well-organized, coordinated, and monitored immunization and pasteurization programs as well as improved nutrition have resulted in a 25-fold reduction in childhood mortality (2).

In developed countries, epidemics of contagious disease have been replaced as leading causes of mortality and morbidity and major consumers of health care resources by congenital malformations, developmental and learning disabilities, and common chronic disease of adulthood and aging. In the U.S., congenital malformations are now the first cause of death in infants under 12 months, the second after injuries in toddlers and young children. Our understanding of the genetic basis of congenital abnormalities and serious childhood disease is growing rapidly and promises to offer solutions to this new public health challenge.

At the same time, dramatic breakthroughs are taking place in the recognition of genes that contribute to common adult-onset disorders such as cancer, diabetes, and heart disease. The task now is to translate this new knowledge of genetics into actions that will improve the public's health.

It is clear that effective implementation of collaborative genetic and public health initiatives can spare the health and lives of tens of thousands of children and adults each year.

II. Genetics and the Human Life Cycle

The preventive potential of medical genetics extends to all branches of medicine at all stages of the life cycle (3).

A. Prenatal

1. Approximately 2-4% of infants (80,000-160,000 per year) are born with birth defects that have serious medical or surgical implications. Many of these birth defects are preventable. About one third of all children hospitalized in tertiary care medical centers have genetic disorders.
2. Intrauterine exposure to alcohol, smoking, cocaine, and other hazardous agents increases the risk for physical and developmental disabilities. Fetal Alcohol Syndrome affects an estimated 7000 infants each year in the U.S. (11). Smoking is associated with small for gestational age infants and cocaine causes placental abruption and prematurity. Well-coordinated public educational efforts targeted to women of childbearing age have the potential for saving thousands and millions of dollars.

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3. Maternal folic acid supplementation prior to and during the pregnancy may prevent the occurrence of open neural tube defects (spina bifida) in approximately 2000 newborns per year. This represents minimal savings of 2000 x $10,000 = $20,000,000 per year (reference 4 and Appendix B-1).

4. Maternal serum multiple marker screening for specific birth defects identifies an estimated 5% of pregnancies at higher risk (approximately 200,000 per year in the U.S.), facilitates their appropriate management, and prevents unnecessary complications of labor and delivery (5).

5. Screening for fetal chromosome abnormalities in the estimated 6% (or 240,000) pregnant women each year who are age >=35 years enables parents not only to make informed decisions, but to plan for timely and effective intervention for affected infants (estimated 5000/year) (Appendix B-2).

6. Prenatal monitoring and management of maternal diseases associated with risk to the fetus result in improved pregnancy outcome. Well-documented examples include the prevention of: 1) mental retardation in offspring of mothers with PKU; 2) congenital malformations and/or metabolic compromise in offspring of diabetic mothers; and, 3) complications in offspring of mothers with prenatal infections (TORCH, HIV, etc.).

7. Selected use of fetal ultrasound identifies abnormalities, enables appropriate management, and optimizes pregnancy outcome.

B. Perinatal

1. Newborn screening for inherited metabolic disorders identifies 3000 infants each year in the U.S. who are born with diseases such as PKU, hypothyroidism, galactosemia, sickle cell disease, and thalassemia. Rapid detection leads to appropriate treatment and prevents metal retardation, physical disability, and death. For example, special protein-restricted diets instituted soon after birth prevent irreversible mental retardation in infants with PKU. Similarly, recent studies have demonstrated that penicillin prophylaxis saves the lives of infants with sickle cell disease.

2. Birth defect surveillance systems in the states and territories obtain baseline information to monitor changes in the incidence or prevalence of specific types of birth defects in specific locations.

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C. Childhood/Adolescence

1. Approximately 3% of school-aged children are cognitively disadvantaged. An additional number have learning, attention, or behavioral and/or emotional difficulties. Early provision of organized, well-coordinated services for children with special needs prevents later complications in these affected children.

2. Common genetic disorders such as mental illness, diabetes, and metabolic disorders appear in childhood and adolescence.

3. Mass education about alcohol and drug abuse as well as contraception and pregnancy planning can prevent unfavorable consequences in thousands of future offspring.

D. Adulthood

1. Genetic issues associated with the childbearing years include pregnancy losses and pregnancies at risk for an unfavorable outcome. Appropriately designed population screening to detect carriers of serious genetic disorders such as Tay-Sachs disease (1 in 30 Ashkenazi Jews are carriers) enables couples to make informed reproductive decisions.

2. Adulthood is associated with appearance by common disorders of great public health significance including hypertension, heart disease, diabetes, and cancers; all of which have a genetic component. For example, the recent identification of genes which, when mutated, increase the risk for breast cancer, offers the possibility of presymptomatic screening for this disease which has a cumulative lifetime risk of 1 in 8 women (6,7).

3. Mental illness including schizophrenia and manic-depression have genetic components and the search is underway to identify the genes involved.

4. Late onset and degenerative diseases with known genetic determinants include Huntington and Alzheimer diseases.

The dramatic breakthroughs in genetic technology and the resulting expansion of molecular diagnostics, make it critically important that we pay attention to cultural differences, quality assurance at all levels, and the active involvement of consumers and families in all genetically related services and deliberations (8). There are important ethical issues to be addressed as screening for late onset and degenerative diseases becomes available to the public.

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Thus, the medical, economic, and social impact of genetically determined disorders is already enormous and their psycho-emotional implications are currently unfathomable. The potential for prevention management, and alleviation of suffering is already a public health issue of significant magnitude. It pales, however, in comparison to the increased needs anticipated within the next few years.

III. Implications of Human Genome Research For Delivery of Genetic Services

In the immediate future, the Human Genome Project (HGP) will result in the identification of an increasing number of disease-causing genes leading to better risk assessment and diagnosis for thousands of genetic disorders. Strategies for prevention, management, and treatment of genetic diseases will impact ever larger numbers of individuals, families, and populations.

No adequate infrastructure exists to process the flood of knowledge 'trickling down' from the HGP to the professional and lay public. Yet the anticipated need and demand for genetic services will undergo a significant expansion within the next three to five years as awareness of the new genetic information increases. Millions of dollars are being directed toward the support of human genome research and its ethical, legal, and social implications. It is clear that similar support is already essential for training and service delivery, including quality improvement (QI) of genetic services for the public's health.

Clinical guidelines are needed to define clearly the quality of care delivered by genetic service providers, such as clinical and laboratory geneticists and genetic counselors. In addition, primary care providers such as those in obstetrics, pediatrics, internal medicine and family practice, as well as specialists in areas such as oncology, surgery, and neurology, may need guidance if they are to participate in the initial workup and ongoing management of patients and families affected by or at risk for genetic disease.

IV. Public Awareness of Genetics: The Challenge For Public Health

The media quickly recognized that genetics-related issues have an impact on a broad segment of the population. In doing so, it became obvious that genetic issues are public health issues. Rarely a month passes without a dramatic discovery in medical genetics. Such breakthroughs raise hopes for cures in many affected individuals and their families. Hence the crucial need for timely and accurate information about the significance of each discovery for the treatment of human disease.

Unfortunately, the current level of understanding and appreciation of the importance of genetic disorders by many health care providers has lagged behind the recent explosion of knowledge due to:

1. Genetic disorders, while cumulatively common, are individually rare, and therefore, individual practitioners may encounter only a few affected families during a lifetime of experience.

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2. Traditionally, modern medicine is oriented toward the individual while the specialty of genetics requires consideration of the extended family as a unit.

3. Genetic disorders are usually permanent and often accompanied by chronic medical and psychosocial problems. They are occasionally disfiguring and perceived as stigmatizing by families and society. Patients and families are frequently reluctant to discuss their concern with their own family members and with their health care providers.

4. Genetic evaluations (e.g. pedigree analysis, cytogenetics, DNA testing) of individuals and families are complex and highly technical procedures for which few physicians or other health care providers are adequately trained to perform or interpret.

5. Genetic evaluations are time-consuming. When they involve multiple family members who may be geographically dispersed, they are logistically complicated.

6. Population screening (e.g. prenatal, newborn, carrier screening) are usually developed and implemented by state agencies with little involvement of primary health care providers.

7. Genetic services which are still frequently documented under the label genetic 'counseling' are rarely seen as essential by health care providers or third party payers. Few practitioners are aware of the reasoning behind accurate and appropriate referrals for genetic services.

8. Documentation of the benefits of genetic services, apart from newborn screening activities, has been difficult and incomplete, hence their importance is not recognized.

9. Although genetics has meaningful potential for the prevention of birth defects and other disorders, prevention is equated by many with elective abortion of handicapped children alone.

Clearly, genetics issues have achieved public health dimensions. The genetics and public health communities must collaborate in educating professionals and the general public about the impact of genetic issues regarding the health of the general population. Such efforts entail defining the role of public health agencies in facilitating access to genetic services for all families and populations.

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Each state and territory should have a plan for an organized and well-documented system of genetic services based on a prior needs assessment as described in sections IC and VI. The following should be addressed in developing these individual plans as described in detail in subsequent sections of this document:

I. Organization and Administration
II. Prevention
III. Services
IV. Research
V. Education
VI. Data Collection and Documentation
VII. Funding

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GUIDELINES FOR CLINICAL GENETIC SERVICES FOR THE PUBLIC'S HEALTH

I. Organization and Administration

A. State/Territorial Genetics Coordinator/Educator. Each state should identify a genetics unit or, at least, a full-time genetics coordinator/educator with a background in service delivery, genetics, and public health issues. The responsibilities of the coordinator should include:

1. Facilitating communication among all existing genetic services in the state/territory.
2. Familiarity with all aspects of clinical and laboratory components of genetic services including:
   a. prevention
   b. dissemination of information (training and education programs)
   c. needs and resources
   d. mechanisms of reimbursement
3. Understanding how genetic services are distributed within their state and promoting the accessibility of these services to all who need them.
4. Identifying needs for additional genetic services in their state.
5. Understanding existing data collection programs and addressing additional needs.
6. Monitoring state legislation and regulatory efforts directed at genetic issues.
7. Familiarity with recognized professional standards for clinical and laboratory personnel, facilities, and genetic services.
8. Monitoring all contracts related to state-funded genetic services.
9. Collaborating closely with the State/Territorial Genetics Advisory Council (see section IB below).

B. State/Territorial Genetics Advisory Council. Each state/territory should develop mechanisms for involvement of genetics providers (clinical, laboratory, educational), consumers, and others in a State/Territorial Genetics Advisory Council. The Council, together with the State Genetics Coordinator or genetics unit representative, assists in the development of the State/Territorial Plan outlined in section IC below.

C. State/Territorial Plan for Provision of Genetic Services. The plan should include the following:

1. Assessment. A description of the:
   a) state/territory (geography, industry, etc.)
   b) demographic parameters (population distribution, birth rate, etc.)
   c) state public health and genetics-related systems
   d) system for data collection
   e) system for evaluation of genetic services and educational activities

DRAFT

2. Policy Development
    a) overview of legislative initiatives, etc.
    b) mechanisms of funding/reimbursement of genetics services

3. Assurance
    a) network of genetics services
    b) system of prevention services
    c) network of educational activities
    d) system for periodic review of genetics services
    e) framework of existing quality assurance (QA) measures for clinical and laboratory genetic services

D. Structure of the State/Territorial Genetic Services Network. The genetic services network within a state may include several levels and types of services.
(Abbreviations: MDG = MD geneticist
MSGC = MS genetic counselor
PhDMG = PhD medical geneticist)

1. Levels of Services
    a) genetics unit of the State Health Department
    b) large, comprehensive genetics center (public, private, academic, etc.)
    c) genetics unit of a comprehensive managed health care facility
    d) resident (as opposed to visiting) genetics unit within a primary health care facility (i.e., satellite or independent clinics) including MDG, MSGC, PhDMG, others
    e) resident MSGC and/or PhDMG with periodic visits by MDG (outreach clinics)
    f) periodic visits by MSGC, MDG, and other staff with local coordinators at outreach clinics
    g) genetics clinics in the private sector conducted by trained MD geneticists
    h) MSGC and/or PhDMG within single disease/medical specialty setting
    i) other

2. Types of Services
    a) FAMILY FOCUSED
        1) state-of-the-art diagnostic, management, support, and counseling services to patients/families at all stages of the life cycle
        2) appropriate specialty programs
        3) evaluation

DRAFT

b) POPULATION BASED

1) prenatal screening and follow-up
2) newborn screening and follow-up
3) birth defects monitoring and follow-up
4) teratogen information services and outcome evaluation
5) screening and/or evaluation in childhood and adult populations
6) screening and/or evaluation of selected populations, e.g., stillborns, others
7) educational services for professionals and the general public
8) data collection
9) evaluation

E. Assurance. The organization of genetic service networks must assure the following:

1) availability of all genetic services including comprehensive evaluation, diagnostic testing at all levels, counseling, treatment, management, and follow-up for all members of the population, irrespective of ability to pay, language differences, or education level
2) education of the professional and general population at all levels about important advances in genetics
3) development of an efficient referral system providing the population in need with the appropriate services
4) quality of service in compliance with accepted guidelines of laboratory and clinical services issued by organizations such as the American College of Medical Genetics (ACMG) and the College of American Pathologists (CAP).
5) privacy and confidentiality for patients and families
6) adherence to ethical and legal considerations during the provision of services (see the CORN Code of Ethical Principles, reference 9)

F. Funding. Funding of clinical and laboratory genetic services must be available through:

1) Medicaid, Medicare
2) third party carriers
3) newborn screening surcharge
4) state and federal service grants
5) specific disease-related organizations where applicable
6) development and implementation of new CPT codes for genetics (10)

DRAFT

II. Prevention

There are four levels of preventing the deleterious effects of diseases or disorders.

A. <u>Primary Prevention</u> -- the absolute prevention of the occurrence of a birth defect, genetic disorder, or disease. Feasible primary prevention in a public health context are as follows.

1. Pre- and periconceptional folic acid prophylaxis can prevent the primary occurrence of about 50% (2000) neural tube defects per year (4). Each of these infants, who might have been aborted prenatally or who, as a newborn, requires hundreds of thousands of dollars of treatment, services, and support throughout life, can now be born free of this birth defect and lead a normal life. Primary prevention includes education targeted to the relevant professionals and consumers (in this example, gynecologists, obstetricians, and women of childbearing age). Monitoring and evaluation of outcomes is an essential part of a successful primary prevention program.

2. Prevention of prenatal exposure to known teratogenic agents from conception through delivery can prevent the primary occurrence of deleterious effects of alcohol, cocaine, smoking, and other hazardous agents. It is estimated that 7000 infants are born each year with fetal alcohol syndrome and that tens of thousands more are in need of special education, behavioral, emotional, and learning services as a result of fetal alcohol effects (11).

   Teratogen information services (TIS) play an important role in primary prevention. A TIS should be available in each state to provide information to physicians and their patients who are concerned about the risk that a particular agent will cause an unfavorable pregnancy outcome. In states without TIS, access to a national or regional information source such as Reprotox (12) and TERIS (13) should be provided. Each TIS should be a part of the national network and comply with national guidelines (14). Collaboration within the existing network has already resulted in research into the teratogenic effects of several agents and has led to the primary prevention of adverse pregnancy outcomes.

3. Awareness and appropriate management of maternal diseases and infections, such as PKU, diabetes, rubella, and toxoplasmosis can result in the primary prevention of birth defects and mental retardation in the newborn. Collaboration between geneticists and physicians specializing in high-risk obstetrics is essential for a successful pregnancy outcome.

DRAFT

4. Genetic counseling, which provides couples with information about their pregnancy risks and reproductive risks and pregnancy options, is another form of primary prevention. Rapid developments in alternative reproductive techniques (preimplantation diagnostics, egg donation, etc.) offer an ever-expanding set of specialized approaches to primary prevention of genetic disorders.

5. In the future, primary prevention will apply to those who are at risk for genetically-determined, adult-onset disorders. For example, DNA-based tests are being developed to detect those at risk for a number of different cancers. Specifically, it is estimated that current methods of screening for specific DNA mutations could detect thousands of women at risk for hereditary breast cancer. The education of professionals and families as well as the development of appropriate surveillance techniques will be essential for primary cancer prevention programs in public health.

B. <u>Secondary Prevention</u> -- Secondary prevention is the prevention of the unfavorable sequelae of already existing disorders or genotypes. Examples include the following.

1. Approximately 3000 affected newborns are identified each year in the U.S. through newborn screening programs for inherited metabolic disease (15). Through detection, treatment, and follow-up, each of these infants is able to lead a life free of the deleterious consequences of their genetic disease. Newborn screening is the best paradigm for a successful genetics public health program. All 50 states and territories screen for PKU and hypothyroidism, identifying about 400 and 1200 infants respectively annually. More than 40 states also screen for sickle cell disease (>1300 cases detected) and some states screen for as many as 7 diseases. Establishing guidelines and the monitoring of newborn screening programs, through state and national committees, provide quality assurance for this highly successful operation (16, 17).

2. Prenatal screening offered through maternal serum markers, fetal ultrasonography, cytogenetic, and/or DNA analyses can not only identify affected fetuses and provide options about pregnancy outcome, but can identify those pregnancies in need of:

    a) special delivery (e.g., Caesarean section to prevent damage to infants with open spine defects)
    b) management of metabolic defects
    c) management of prematurity or intrauterine growth retardation
    d) prenatal intervention, including fetal surgery

DRAFT

3. Screening for genetic disorders includes:

    a) identification of those who have fragile X syndrome and other identifiable disorders
    b) identification, at birth, of genetic disorders and other developmentally disabled birth defects requiring immediate treatment
    c) recognizing hyperlipidemia in the population of young adults as a step toward preventing coronary artery disease
    d) presymptomatic screening for cancers
    e) identification of individuals at risk for adult-onset, neurodegenerative disorders

C. Tertiary Prevention. -- Tertiary prevention aims to ameliorate the unfavorable consequences of existing disorders. For example:

1. educational and other comprehensive services to children and adults with special needs
2. appropriate management of genetic disorders
3. Access to orthotic and other auxiliary devices, dietary supplements, special occupational and physical therapy, ongoing support group services

Collaboration with consumers and the Alliance of Genetic Support Groups is of primary importance, especially in issues of tertiary prevention (18).

In addition to the three traditional levels of prevention outlined above, a 'quaternary' level of prevention involves the ongoing research into genetic diseases by the Human Genome Project, TIS, and other initiatives. Prevention also extends to the prevention of discrimination on the basis of genetic disease or testing by employers, insurers, and peers.

III. Services

A. Types of Services

1. **FAMILY FOCUSED SERVICES**. Genetic clinics serve children and adults at risk because of genetic disorders.

    a) **General Genetic Clinics** provide service to individuals with:

        1) known or suspected genetic disorders
        2) congenital anomalies/birth defects
        3) mental retardation, developmental or behavioral disorders

DRAFT

4) consanguinity or ethnicity associated with increased risk for specific disorders
5) family history of the above

b) **Metabolic Clinics** serve those with:

1) known or suspected inborn errors of metabolism regardless of onset of symptoms
2) a family history of a metabolic disorder
3) other

c) **Single Disease Clinics** are often managed by non-geneticists but requiring professional genetic input, these clinics serve individuals and families with:

1) genetic hematologic diseases (e.g., sickle cell anemia)
2) genetic pulmonary diseases (e.g., cystic fibrosis)
3) genetic neurological, neuromuscular, neurodegenerative diseases (e.g, muscular dystrophy, Huntington disease)
4) birth defects requiring multidisciplinary approaches to management (e.g., craniofacial disorders, spina bifida)
5) cancer
6) other genetic disorders

d) **Prenatal Clinics** focus on those at risk for an unfavorable pregnancy outcome or who have had abnormal prenatal screening results. Examples include:

1) risks associated with advanced maternal age
2) couples with a previous child affected with a genetic disorder or birth defect
3) couples with a family history of a genetic disorder or birth defect
4) couples with multiple pregnancy losses
5) risks associated with maternal illnesses, medications, exposures, or infections
6) pregnancies with abnormal screening test results
7) pregnancies identified as abnormal by fetal ultrasonography
8) other

DRAFT

2. POPULATION-ORIENTED SERVICES/SCREENING THROUGHOUT THE LIFE CYCLE

a) Prenatal screening:

1) maternal serum alpha-fetoprotein and associated marker screening
2) maternal infections
3) maternal disease (e.g., diabetes)
4) carrier status (e.g., Tay-Sachs, sickle cell anemia)
5) fetal ultrasonography

b) Newborn screening and follow-up as appropriate in each state [see Newborn screening guidelines (16, 17)]

c) Childhood screening for genetically determined developmental disabilities, sensory deficits, and other disorders

d) Adult screening:

1) presymptomatic testing
2) diagnostic testing/screening
3) carrier testing/screening for neurodegenerative diseases in selected populations
4) cancer susceptibility
5) diseases related to aging (e.g., heart disease, Alzheimer disease)

3. CLINICAL LABORATORY SERVICES

Centers/clinics should have easy access to facilities for analyzing specimens for genetic studies, including, but not limited to, blood, urine, tissue, and amniotic fluid. Transport of specimens for analysis should be arranged and a tracking system maintained.

Laboratory services (10) should be provided by genetic centers and should include cytogenetic, biochemical, and molecular laboratory services as follows:

a) Cytogenetic laboratories should be able to complete cytogenetic analysis and provide interpretation of studies of lymphocytes, amniotic fluid cells, and other tissues for the purpose of determining the number and structure of the chromosomes.

DRAFT

b) Biochemical genetics laboratories should have the capacity for analysis and interpretation of test results for alpha-fetoprotein, selected enzymes, substrates, metabolic reactions, structural proteins, hemoglobins, and other biochemical systems.

c) Molecular genetics laboratories should have the capacity to complete specified DNA analysis and interpret results.

d) Requests for biochemical and molecular tests which are unavailable in a state should be referred to regional or national facilities as needed.

Effective communication between patients, clinics, laboratories and primary care physicians must be ensured. Accurate and timely interpretation of laboratory results with supportive explanation, counseling, follow-up, and referrals must be available.

B. Levels of Service. See section I. Organization and Administration, paragraph D.

C. General Facility and Operational Requirements

1. GENERAL FACILITY REQUIREMENTS

a) The facility should be an identifiable unit in an accredited state or other medical school, a hospital, or a clinic accredited by the Joint Commission on Accreditation of Health Care Organizations.

b) The facility should be licensed by the State Department of Health, if such licensure is required for operation, or by any other licensing agency as required.

c) Private facilities should demonstrate compliance with appropriate certifying agencies.

d) The facility should have access to medical support services necessary for diagnosis of genetic or congenital disorders.

e) The facility should include, but not be limited to, an identifiable clinic area with rooms for examination, counseling, management, and evaluation which are appropriately equipped for delivery of services and privacy for patients and/or family.

f) The facility must be accessible to the handicapped.

DRAFT

g) The facility should have its own telephone number or extension through which all services can be accessed.

2. GENERAL OPERATIONAL REQUIREMENTS FOR SERVICES

a) Services should be available and accessible.

b) Admission and referral policies should facilitate entry of the population to be served.

c) The administration and staff of the center should continuously update their knowledge and skills through in-service education programs and attendance at conferences, seminars, and workshops.

d) The center should develop and maintain an active program to monitor the quality of services provided.

e) Input by those using the services ('consumer input') should be routinely obtained for the purpose of planning evaluation of services.

f) Laboratories associated with the genetics unit should participate successfully in available proficiency testing programs.

The centers should ensure effective and efficient administration.

g) Staff meetings should be scheduled at least quarterly with written meeting summaries maintained.

h) The center should maintain written contracts/agreements for all core professional services not directly provided by personnel of the center. Contracts or agreements should include identification of services to be rendered, including, where appropriate, the hours and personnel involved as well as the payment and billing procedures.

i) Centers should maintain written protocols identifying laboratories that will accept specimens for necessary tests, payment methods, unique services, and typical turnaround time used for diagnostic evaluations. A tracking system (log) should be maintained for all specimens.

j) A written admission policy should be available and include: service fees, billing

procedures, and available financial assistance, as well as schedulers of clinic and office hours.

k) No individual with a suspected genetic condition should be refused genetic services because of any disability or medical condition.

l) State programs should provide support to those patients/families who are unable to pay.

D. Genetic Health Care Professionals

1. STAFF

The following staff should be available or accessible to provide genetic services at each center. Alternatively, expert consultation must be available by referral to another institution. Genetic centers typically have as their director a medical geneticist who heads a staff consisting of one or more of the following genetic health care professionals.

In this section and in the corresponding sections in Appendix C, superscript numbers are used to explain the sources of the wording:

[1]*The wording for categories a,b,d,e and f is taken verbatim from the American Board of Medical Genetics (ABMG) Bulletin of Information, 1996 (19).*
[2]*Category c is from the American Board of Genetic Counseling (ABGC) Bulletin of Information, 1996 (20).*
[3]*Categories g and h are from International Society of Nurses in Genetics (ISONG) Standard of Practice, DRAFT, 1996 (21).*
[4]*Paragraphs are abstracted from The ABMG Bulletin of Information, 1996 (19).*
[5]*Paragraphs are abstracted from document ABGC Bulletin of Information, 1996 (20).*
[6]*Association of Cytogenetic Technologists (ACT) (22).*

a) Clinical Geneticist[1] An individual who holds an MD or DO degree and demonstrates competence to provide comprehensive diagnostic, management, and counseling services. Clinical geneticists come from a variety of disciplines including pediatrics, internal medicine, obstetrics/gynecology, ophthalmology, and dentistry.[4]

DRAFT

b) PhD Medical Geneticist[1] An individual with a PhD degree who works in association with a medical specialist, is affiliated with a clinical genetics program, serves as a consultant to medical and dental specialists, and/or serves in a supervisory capacity in a medical genetics program. PhD Medical Geneticists have PhD's in a variety of disciplines including biochemistry, molecular biology, epidemiology, and mathematics.[4]

c) Genetic Counselors[2] Genetic Counselors are health professionals who are academically and clinically prepared to provide genetic counseling services to individuals and families seeking counseling information about the occurrence, or risk of recurrence, of a genetic condition or birth defect. They are prepared to practice as an integral part of a genetic services delivery team. Genetic Counselors come from a variety of backgrounds including biology and other basic sciences, social work, and nursing.[5]

d) Clinical Cytogeneticist[1] An individual with a doctoral degree (MD, DO, PhD) who is competent to perform and interpret cytogenetic analyses relevant to the diagnosis and management of human genetic disease and can act as a consultant regarding laboratory diagnosis for a broad range of disorders.

e) Clinical Biochemical Geneticist[1] An individual with a doctoral degree (MD, DO, PhD) who is competent to perform and interpret biochemical analyses relevant to the diagnosis and management of human genetic disease, and who acts as a consultant regarding laboratory diagnosis of a broad range of disorders.

f) Clinical Molecular Geneticist[1] An individual with a doctoral degree (MD, DO, PhD) who is competent to perform and integrate molecular analyses relevant to the diagnosis and management of human genetic disease, and who acts as a consultant regarding laboratory diagnosis of a broad range of disorders.

g) Cytogenetic Technologist[6] An individual with a minimum of a BS degree who demonstrates competence to provide cytogenetic analysis in a clinical diagnostic laboratory under the supervision of a laboratory director qualified in clinical cytogenetics.

h) Genetic Nurse[3] An individual who provides nursing care for a client population with a specific genetic condition or a need for a specific genetic service. Genetic Nurses are licensed registered nurses who have received genetic continuing education.

DRAFT

i) Advance Practice Nurse in Genetics[3] An individual with a MS or PhD in nursing who has completed graduate level genetics course work and assures possession of current knowledge through participation in genetic continuing education.

j) Perinatologist/Obstetrician or other physician must be accessible for referral; conducts all invasive prenatal diagnostic studies.

k) Other medical/surgical specialties and subspecialties available through a clinical genetic center should include, but not be limited to: pediatrics, obstetrics and gynecology, pathology, psychiatry, neurology, and orthopedics.

l) Other staff available through a clinical genetics center should include, but not be limited to: psychologist, social worker, nutritionist, occupational and physical therapists, special education experts, foreign language translators, and interpreters for the hearing impaired.

2. STAFF CREDENTIALS

a) The following providers of genetic services: Clinical Geneticists; PhD Medical Geneticists; Genetic Counselors; Cytogenetic, Biochemical, and Molecular Genetic Laboratory Directors; and Cytogenetic Technologists should be certified, as appropriate, by the American Board of Medical Genetic (ABMG), the American Board of Genetic Counseling (ABGC), the National Certification Agency for Medical Laboratory Personnel (NCA), or be board eligible. Eligible status for certification may be maintained for no more than two administrations of the Board's examination.

b) Physicians should be licensed by the state and be board certified or board eligible in their speciality area.

c) A Clinical Geneticist should be a licensed physician.

d) Medical directors should be licensed physicians.

e) Cytogenetic Technologists should be certified by NCA and licensed by the state as appropriate.

f) All other professionals should be licensed by the state, as appropriate.

DRAFT

g) If no license requirements exist, the professional should be certified (accredited) by the appropriate national organization.

E. <u>Components of a Genetic Evaluation</u>. The following clinical genetic services should be provided, on site, unless otherwise specified, by appropriately credentialed professionals.

1. **GENERAL CLINICAL GENETIC SERVICES** should include, as appropriate:

a) review of medical records and history
b) analysis of family history/pedigree construction
c) physical examination including growth and development assessment
d) access to diagnostic testing including, but not limited to, radiological procedures (X-rays, magnetic resonance imaging [MRI])
e) evaluation and diagnosis
f) specimen collection for diagnostic studies/evaluations (inpatient and outpatient)
g) risk assessment
h) genetic counseling and education including anticipatory guidance for patient/family, support
i) management/treatment of genetic diseases or conditions
j) coordination of medical/surgical consultation(s) and/or referral(s) for supporting services as appropriate
k) short- or long-term follow-up as needed
l) staff should be familiar with practice guidelines developed for specific disorders or groups of disorders by the American College of Medical Genetics subcommittee on practice guidelines. Examples include the dysmorphic newborn, the developmentally delayed child, stillborns, and individuals or families with breast cancer (23).

2. **PRENATAL GENETIC SERVICES** for problems relating to increased risk should, as appropriate, include:

a) review of medical records and history
b) analysis of family history/pedigree construction
c) physical examination
d) other screening and/or diagnostic procedures, including but not limited to, cytogenetic, biochemical, and molecular testing for patient/family
e) risk assessment
f) genetic counseling, education, and support for patient and family
g) management/treatment of genetic diseases or conditions

DRAFT

h) coordination of medical consultation(s) and/or referral(s) for services, as appropriate
i) The center should provide or arrange for radiological or other diagnostic testing, including but not limited to, high resolution ultrasonography, fetal echocardiography, amniocentesis, chorionic villus sampling, tissue biopsy, X-ray, magnetic resonance imaging (MRI), CT scan, and cordocentesis.
j) follow-up, communication of results, further consultation as needed
k) staff familiarity with Practice Guidelines (see section E.1.1)

3. **PRIOR TO ANY TESTING PROCEDURE**, every person seeking services will be advised of:

   a) the nature and purpose of the procedure and its implications
   b) benefits and risks involved
   c) the opportunity to decline participation
   d) estimated fees, charges, and billing procedures

4. **A WRITTEN SUMMARY/LETTER** of the results of a genetics evaluation and its implications should be sent to the referring physician(s). A copy should be placed in the patient's chart and, where possible, the results sent in the form of an understandable letter to the patient/family. The opportunity to discuss all issues with a supportive, informed professional should be offered. Relevant literature and support educational materials should be available.

5. **APPROPRIATE REFERRALS** should be made to the following:

   a) medical specialties/subspecialties
   b) care management services
   c) social services
   d) early intervention services
   e) home health services
   f) national/local family support groups (18)

F. Patient Records

1. Confidentiality of records must be protected and written procedures regarding access to records must be known by all staff.

2. It must be standard operating procedure to obtain necessary releases and send a written report on each patient and/or family to the referring physician/professional.

DRAFT

3. Prior to releasing a patient's report to any other professional service provider, a specific written release must be signed by the patient/parent.

4. Genetic records should be maintained as part of the permanent medical record for each patient. Records should be retained in confidential files which are locked or otherwise secured. Records should be accessible to staff of the center and consultants and should include, but not be limited to:

    intake information
    medical history
    laboratory test results
    diagnostic reports
    counseling summary report
    plan of care (as indicated)
    record of services at other facilities
    informed consent forms
    written releases
    referral information

G. Human and Legal Rights

1. There must be a written informed consent policy for all invasive evaluations and treatment procedures.

2. The center should arrange for foreign language interpreters and interpreters for the hearing impaired when necessary.

3. The center should not discriminate through admission policies, hiring policies, or promotional opportunities on the basis of race, religion, ethnic origin, sex, or handicapping condition.

4. Institutional review board guidelines must be observed when conducting research.

5. Patients/families must be informed about ownership of stored biological specimens and all relevant issues related to such specimens.

6. Patients and family should have access to information about the hospital's or institution's bio-ethics committee and its deliberations relevant to the patient/family's specific situation as applicable.

DRAFT

H. Quality Assurance

1. The administration and staff of the center must demonstrate a commitment to quality care:

    a) There should be a written statement of mission and goals for the center

    b) There should be a designated administrator for the service unit.

    c) The administration and staff of the center should continuously update their knowledge and skills through in-service educational programs and attendance at conferences, seminars, and workshops.

    d) The center should develop and maintain an active program to monitor the quality of services provided.

    e) Consumer input (e.g., patient satisfaction) should be routinely obtained for the purpose of planning and evaluation of services.

    f) Laboratories associated with the genetic unit shall participate successfully in the appropriate proficiency testing programs.

IV. Research[1]

A. The state genetics unit and/or the genetics coordinator together with the advisory council, should be aware of educational sessions, media releases or other vehicles, whereby results from research are communicated accurately and appropriately to those professionals and the general public for whom they are relevant.

B. Patients and families should be given the option to participate in research studies if desired under the following conditions:

    1. All research projects/protocols involving human subjects have undergone review and obtained approval of the Institutional Review Board.

    2. Patients/families are fully aware that they are participating in research and most likely will receive no answers or results from their tests.

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[1]Research training for genetics professionals is not considered to be relevant to this document.

DRAFT

3. Patients/families have given informed consent after receiving an accurate and understandable explanation of the procedure in question, its risks, benefits, and other implications.

4. Privacy/confidentiality of the patient's participation and results are ensured.

C. State genetics units should be encouraged to participate in collaborative, public health-related research projects, e.g., TIS-initiated research, epidemiologic data collection, etc.

V. Education

In the broadest sense, education is provided at several levels of sophistication to different target audiences. Levels of education include:

A. **AWARENESS** - i.e., a "flash" of information about the existence of a subject. For example:

1) BRCA1 is a recently recognized gene which might in the future enable the detection of some individuals at risk for developing breast cancer.

2) Pregnancies which are exposed to hazardous environmental agents might be at higher risk for an unfavorable outcome.

3) Disorders which occur within several members of a family might be hereditary.

4) Taking folic acid prior to and during pregnancy can prevent some birth defects.

"Awareness increasing" activities might include TV spots, flyers, news conferences, notices/posters in public (or clinical) locations, individual items mentioned within educational sessions.

Target audiences for awareness are broad and include the general public (all ages), teachers, media personnel, school children, nongenetics professionals, others. The public health agencies within states can take responsibility for increasing the awareness among professionals and the public when important issues arise. It is they who produce flyers, posters, and TV flashes.

DRAFT

B. **INFORMATION** - Information implies a more detailed level of knowledge than does awareness. For example:

1) BRCA1 may be a tumor suppressor gene which, if mutated, might predispose to breast and/or ovarian cancer.

2) If a physician, patient, or other care giver is concerned about hazards to a pregnancy, teratogen information services can provide more information regarding a particular agent.

3) There are multiple mechanisms and patterns of inheritance; for example, not all familial disorders are genetic.

4) Which birth defects might be prevented by folic acid ingestion, what dose is recommended, and to whom does this information apply.

Target audiences for information include teachers at all levels: grades 6-12, college; topic oriented non-genetics professionals, medical students, and other trainees; consumers; relevant parents/families; media personnel; and specific interest groups.

Public health agencies support workshops, produce brochures, etc. and are generally involved with the information component of education also.

C. **INSTRUCTION** - Instruction implies providing more complicated information such as:

1) the state of the art of BRCA1 screening, including the molecular structure of the gene and how it functions to cause cancer, who should be offered screening, what results can be expected, and how are they interpreted.

2) mechanisms of the effects of alcohol exposure during pregnancy

Instruction occurs during single topic educational sessions, workshops, "hands-on" discussions, and CME conferences. Target audiences for instruction are usually those for whom the subject is personally or professionally relevant. These audiences include genetics and non-genetics service providers, MD specialists, teachers, students, allied health professionals, creators of media teaching tools, specific at-risk populations, support groups, parents, patients, and others.

Evaluation should be a required component of each level of education including awareness (less important), informational and instructional activity (very important).

DRAFT

D. **TRAINING** - is a long term activity, the anticipated result of which is the emergence of individual experts within a specific area. It includes training of a) future genetics professionals at all levels and in all areas of expertise, and b) existing genetics professionals in new areas of their field. In the current climate of managed care, it is recommended that MDs in other areas of expertise become acquainted (e.g., through short term fellowships, independent study courses, collaboration, training sessions, etc.) with the basic principles of modern genetics. It is recommended that this occur principally with primary care physicians. Other care givers within specific settings also require additional training to become experts in their own area of activity.

Participants in training programs are eligible for accreditation and certification by national regulatory bodies, e.g., ABMG, RRC, ABGC, NCA, etc. State public health agencies have no known role in training of genetics professionals, unless it is formal, subject specific training.

VI. Documentation of Needs and Services

A. DATA SOURCES

At the state level, numerous public health databases collect information concerning individuals with genetic diseases. These data systems are generally administrative in nature, providing documentation of vital status, eligibility for and utilization of program services, and, in some instances, monitoring or surveillance functions. For assessment of genetics in public health, the purpose and primary functions of each database must be considered in the initial assessment of its utility for this purpose. For example, birth defects registries are now in existence in about half of the states. These registries vary greatly in design, case ascertainment methods, and primary uses.

A partial list of potential statewide data sources for genetics and public health would include:

1. state level clinical genetics databases (at a minimum, the CORN Minimum Data Set) (24)
2. newborn screening data
3. vital statistics: birth, fetal death, and death certificates
4. statewide hospital discharge data (linked at the individual level across in-patient stays)
5. Medicaid/Medicare eligibility, claims, and provider datasets
6. statewide/local cytogenetics registry data
7. statewide birth defects registry (a few areas have local registries)

DRAFT

8. statewide/local population based cancer/tumor registries or reporting systems
9. other registries (developmental disabilities surveillance, support group registries, specialized support group registries)
10. directories of genetics service providers and referral sources
11. cytogenetic laboratory databases collected by the ACT
12. federal census data (primarily for population denominators and as basis for population projections)
13. Special surveys and research projects include:
    a) Pregnancy Risk Assessment Monitoring System (CDC - ongoing, many but not all states participate)

    b) National Maternal and Infant Health Survey (NCHS - most recent is 1988)

    c) Behavioral Risk Factor Surveillance System (CDC - annual, almost all states participate)

    d) National Survey of Family Growth (NCHS)

B. **LINKAGES**

There are a number of essential linkages which should occur at every state level for the purpose of monitoring occurrence of specific genetic diseases, outcomes in infants/children with those diseases, and assessment of service utilization and efficiency of service delivery. These include:

1. linkage of birth and death certificates for all deaths up to age six
2. linkage of birth defects and tumor registry data for all pediatric cancer cases
3. routine linkage of birth defects registry records with vital statistics (births, fetal deaths and deaths)
4. routine linkage of statewide inpatient hospital discharge records with birth certificates
5. routine linkage of newborn screening records with birth certificates
6. linkage of (MSAFP/AFAFP/triple screen, etc.) screening database with vital statistics (if such a database exists)
7. linkage, at least in the form of numerator/denominator ratio data, between the statewide clinical genetics services database and birth/fetal death certificates
8. systems for direct referral from clinical genetics to early intervention services for

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infants and children under the age of 3 (Part H: Public Law 99-457), Children with Special Health Care Needs (CSHCN), Supplemental Social Insurance (SSI) and other services/entitlements for children/families with disabilities associated with genetic disorders or diseases.

VII. Funding

All State Public Health Agencies are responsible for funding several aspects of genetics services. However, the mechanisms, organization and types of funding differ among states, hence details cannot be presented. Types of funding in most states include:

1. Medicaid, Medicare
2. third party carriers, including employers/insurers
3. newborn screening surcharge
4. state and federal grants
5. specific disease or disease group organizations, e.g., Muscular Dystrophy Association, Cystic Fibrosis Foundation
6. specific sources for individuals with developmental disabilities, e.g., Bureau for Children with Special Health Care Needs, "Crippled" Children's organizations, etc.

New CPT codes for genetic services are being developed which will result in improved reimbursement for genetics (10).

Third party payment for genetic services is often a problem. There are a considerable number of patients in need of and/or receiving genetics services who a) have no insurance coverage; or b) do not wish to inform the insurance carrier about the disorder for fear of discrimination.

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APPENDICES

A. CORN AND THE REGIONAL NETWORKS

B. CALCULATIONS

C. DESCRIPTIONS OF GENETIC PROFESSIONALS

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APPENDIX A

CORN AND THE REGIONAL NETWORKS

Council of Regional Networks for Genetic Services (CORN)
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APPENDIX B

CALCULATIONS

B-1. ~4,000,000 live births/year
Incidence of NTD = 1/1000
50% preventable by folic acid prophylaxis
50% of 4000 = 2000
If only $10,000 cost/affected infant, then 2000 x $10,000 = $20,000,000

B-2. 6% of 4 million pregnancies = 240,000
Incidence of nondisjunction at age 35-45 ≅ 2%
2% of 240,000 = 5000 infants

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APPENDIX C

DESCRIPTIONS OF GENETIC PROFESSIONALS*

CLINICAL GENETICIST:

An individual who holds an MD or DO degree and demonstrates competence to provide comprehensive diagnostic, management, and counseling services.

Competence in this area implies that the individual possesses:

- diagnostic and therapeutic skills in a wide range of genetic disorders;
- an appreciation of the heterogeneity, variability, and natural history of genetic disorders;
- the ability to elicit and interpret individual and family histories;
- the ability to integrate clinical and genetic information and appreciate the limitations, interpretation, and significance of specialized laboratory and clinical procedures;
- the expertise in genetic and mathematical principles to perform risk assessment;
- the skills in interviewing and counseling techniques required to: 1) elicit from the patient or family the information necessary to reach an appropriate conclusion; 2) anticipate areas of difficulty and conflit; 3) help families and individuals recognize and cope with their emotional and psychological needs; 4) recognize those situations requiring psychiatric referral; and 5) transmit pertinent information effectively (i.e. in a way that is meaningful to the individual or family);
- the knowledge of available health care resources required for appropriate referral.

Clinical Geneticists come from a variety of disciplines including pediatrics, internal medicine, obstetrics/gynecology, ophthalmology, and dentistry. Certification is provided through the American Board of Medical Genetics.

Ph.D. MEDICAL GENETICIST:

An individual with a Ph.D. degree who works in association with a medical specialist, is affiliated with a clinical genetics program, serves as a consultant to medical and dental specialists, and/or serves in a supervisory capacity in a medical genetics program.

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Competence in this area implies that the individual possesses:

- the ability to elicit and interpret individual and family histories;
- an appreciation of the heterogeneity, variability, and natural history of genetic disorders;
- the ability to integrate clinical and genetic information in order to appreciate the limitations, interpretation, and significance of specialized laboratory and clinical procedures;

- the expertise in genetic and mathematical principles to perform complex risk assessments, to interpret pedigree analysis (both segregation and linkage) and to understand the principles of genetic etiology;
- the skills in interviewing and counseling techniques required to: 1)elicit from the patient or family the information necessary to reach and appropriate conclusion; 2) anticipate areas of difficulty and conflict; 3) help families and individuals recognize and cope with their emotional and psychological needs; 4) recognize those situations requiring psychiatric referral; and 5) transmit pertinent information effectively (i.e. in a way that is meaningful to the individual or family).

Ph.D. Medical Geneticists have Ph.D.'s in a variety of disciplines including biochemistry, molecular biology, epidemiology, and mathematics. Certification is provided through the American Board of Medical Genetics.

CLINICAL CYTOGENETICIST:

An individual with a doctoral degree (M.D., D.O., Ph.D.) who is competent to perform and interpret cytogenetic analyses relevant to the diagnosis and management of human genetic diseases and can act as a consultant regarding laboratory diagnosis for a broad range of disorders.

Competence in this area implies that the individual possesses:

- the ability to supervise and direct the operations of clinical cytogeneticists diagnostic laboratory;
- an appreciation of the heterogeneity, variability, and natural history of genetic disorders;
- diagnostic and interpretive skills in a wide range of cytogenetic problems;
- the ability to appropriately communicate cytogenetic laboratory results in the capacity of consultant to other clinicians or directly to patients in concert with other appropriate clinicians or genetic counselors.

Clinical Cytogeneticists generally have a Ph.D. in molecular biology, molecular genetics, or cytogenetics. Certification is provided through the American Board of Medical Genetics.

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CYTOGENETIC TECHNOLOGIST

An individual with a minimum of a BS degree who demonstrates competence to provide cytogenetic analysis in a clinical diagnostic laboratory under the supervision of a laboratory director qualified in clinical cytogenetics.

Competence in this area implies that the individual possesses:

- the ability to process specimens for cytogenetic analysis, including the knowledge to select culture, harvesting, slide preparation, and staining techniques appropriate to each specimen type;
- the skill to: 1) select the appropriate metaphases, identify chromosomal abnormalities, assess difficulties with analysis, and prepare accurate karyotypes; and 2) summarize the results and prepare reports which are reviewed by the laboratory director or another clinical cytogeneticist;
- knowledge of general laboratory skills, quality control and quality assurance procedures, and knowledge of the general principles of biology and genetics, including the principles of clinical cytogenetics.

Cytogenetic Technologists come from a variety of backgrounds and include biologists, chemists, and clinical laboratory scientists. Certification as a Clinical Laboratory Specialist in Cytogenetics is provided through the National Certification Agency for Medical Laboratory Personnel (NCA) and is maintained through participation in continuing education.

CLINICAL BIOCHEMICAL GENETICIST

An individual with a doctoral degree (M.D., D.O., Ph.D.) who is competent to perform and interpret biochemical analyses relevant to the diagnosis and management of human genetic disease, and who acts as a consultant regarding laboratory diagnosis of a broad range of disorders.

Competence in this area implies that the individual possesses:

- the ability to supervise and direct the operations of a clinical biochemical diagnostic laboratory;
- broad knowledge of: 1) basic biochemistry and biology; 2) the application of biochemical techniques to the diagnosis and management of genetic diseases; and 3) the etiology, pathogenesis, clinical manifestations, and management of human inherited biochemical disorders;

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- the ability to appropriately interpret and communicate biochemical laboratory results in the capacity of consultant to other clinicians or directly to patients in concert with other appropriate clinicians or genetic counselors.

CLINICAL MOLECULAR GENETICIST:

An individual with a doctoral degree (M.D., D.O., Ph.D.) who is competent to perform and integrate molecular analyses relevant to the diagnosis and management of human genetic diseases, and who acts as a consultant regarding laboratory diagnosis of a broad range of disorders.

Competence in this field implies that the individual possesses:

- the ability to supervise and direct the operations of a clinical molecular genetics diagnostic laboratory;
- the ability to perform a variety of diagnostic assays;
- a broad knowledge of: 1) basic molecular biology and genetics; 2) the application of recombinant DNA techniques and linkage analysis to the diagnosis of genetic diseases; and 3) the etiology, pathogenesis, clinical manifestations, and management of human genetic disorders;
- the ability to appropriately interpret and communicate molecular diagnostic laboratory results in the capacity of a consultant to other clinicians or directly to patients in concert with other clinicians or genetic counselors.

Clinical Molecular Geneticists come from a variety of backgrounds and include medical geneticists and individuals with a Ph.D. in molecular genetics or molecular biology. Certification is provided through the American Board of Medical Genetics.

GENETIC COUNSELOR:

Genetic Counselors are health professionals who are academically and clinically prepared to provide genetic counseling services to individuals and families seeking counseling information about the occurrence, or risk of recurrence, of a genetic condition or birth defect. They are prepared to practice as an integral part of a genetic services delivery team.

Competence in the area of genetic counseling implies that the individual possesses the ability to:

- elicit and interpret individual, family, medical, developmental, and reproductive histories;

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- determine the mode of inheritance and risk of transmission of genetic conditions and birth defects;
- discuss the mode of inheritance, features, natural history, means of diagnosis, and management of these conditions;
- identify, coordinate, interpret, and explain genetic laboratory tests and other diagnostic studies;
- assess psychosocial factors, recognizing social, educational, and cultural issues;
- evaluate the client's/family's responses to the condition or risk of recurrence and provide client-centered counseling and anticipatory guidance;
- communicate information to family members in an understandable manner;
- facilitate informed decision making about testing, management, and reproductive alternatives; identify and effectively utilize community resources that provide medical, educational, financial, and psychosocial support and advocacy; and provide accurate written documentation of medical, genetic, and counseling information for families and health care professionals.

Genetic Counselors come from a variety of backgrounds including biology and other basic sciences, social work, and nursing. Genetic Counselors are certified through the American Board of Genetic Counselors.

ADVANCED PRACTICE NURSE IN GENETICS

An individual with a M.S. or Ph.D. in nursing who has completed graduate level genetics course work and assures possession of current knowledge through participation in genetic continuing education.

Competence in this area implies that an individual possesses the ability to utilize the nursing process in practice delivery as listed under genetic nurse as well as have the ability to:

- use counseling skills and interventions to assist clients in understanding genetic concepts, their implications to the client and family, and assist the client in adjusting to their perceived burden;
- provide consultation to health care providers and others to influence the plan of care and enhance the abilities of others to provide care for patients with genetic conditions;
- participate in the clinical evaluation of clients with genetic conditions;
- guide nurses in the specialized care of client's with genetic conditions; provide expert input into the development, management, and/or evaluation of a multi disciplinary genetic clinical research protocol;
- participate in assessment and deliberation of ethical, legal, and social consequences of existing and predicted genetic services and technologies;

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- provide case management across a variety of settings for genetic clients who have complex health care needs.

Advanced Practice Nurses in genetics come from a variety of nursing disciplines including maternal/child health, oncology, neurology, hematology, endocrine, and others. Steps towards creating a nursing certification examination in clinical genetics in in process. Some genetics Advanced Practice Nurses have become certified as genetic counselors through the American Board of Genetic Counseling.

GENETIC NURSE:

An individual who provides nursing care for a client population with a specific genetic condition or a need for a specific genetic service. Genetic Nurses are licensed registered nurses who have received additional education in the area of genetics.

Competence in this area implies that the individual possesses the ability to:

- collect and examine health data by participating in activities such as performing a physical examination; obtain family, medical, developmental and reproductive histories; collect appropriate laboratory data; inquire into client's desired health outcomes; and assess the client's understanding of the genetic condition;
- establish an appropriate plan of nursing care designed for the genetic client and coordinate that care with other health professionals. Client focused immediate and long term health care needs are determined and used to develop a plan of action;
- implement interventions which may include: 1) heightening awareness about services and health behavios that may reduce the risk of or symptoms of a genetic condition; 2) facilitate successful adaptive responses to disease processes; 3) educate about, administer, and monitor responses to therapies for a genetic condition; 4) advocate for and facilitate access to genetic resources and support groups; and 5) provide or reinforce information about a genetic condition routinely cared for by the nurse;
- evaluate the plan of care based on new data, resources, and the client's changing needs

Genetic Nurses can be found in a diverse number of clinical settings specific to the disorder in question.

Sickle Cell Guidelines from Texas Genetics Networks

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Introduction

Sickle cell disease is a generic term for a group of genetic disorders characterized by the predominance of hemoglobin S (Hb S). These disorders include sickle cell anemia, the sickle beta thalassemia syndromes, and hemoglobinopathies in which Hb S is in association with another abnormal hemoglobin that not only can participate in the formation of hemoglobin polymers but is present in sufficient concentration to enable the red cells to sickle. Examples of the latter disorder include hemoglobin SC disease (Hb SC), hemoglobin SD disease (Hb SD), and hemoglobin S O_{Arab} (Hb S O_{Arab}). The sickle disorders are found in people of African, Mediterranean, Indian, and Middle Eastern heritage. In the United States, these disorders are most commonly observed in African-Americans and Hispanics from the Caribbean, Central America, and parts of South America.[1]

Although the hemoglobinopathies represent one of the major health problems in the United States, and constitute the most common genetic disorder in some populations, screening programs have been slow to add the hemoglobinopathies to their list of screening disorders.[2] New York was the first state to begin universal screening in 1975, followed by Colorado in 1979, and Texas in 1983. Currently, there are thirty-four states with universal screening programs, ten states with selected or pilot programs, and seven states that do not have a hemoglobinopathy program.[3]

During the past ten years, three major incidents have occurred to encourage hemoglobinopathy screening: 1) the 1986 publication of a federally funded, multi-center study showing that prophylactic treatment with penicillin reduced pneumococcal septicemia in infants by 84%, 2) the provision of federal funds in 1988 for Newborn Screening Programs to develop or improve existing hemoglobinopathy programs, and 3) in 1987, the National Institutes of Health sponsored a consensus conference on Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies for the purpose of developing a national position on screening. In the latter case, the conference attendees addressed issues of effectiveness in decreasing morbidity and mortality in newborns by screening for sickle cell disease, screening techniques to be used and their efficacy, major factors to be considered in hemoglobinopathy screening, optimal follow-up and management of infants identified with hemoglobinopathies, and the direction of future research. The conference statement concluded that every child should be screened for hemoglobinopathies to prevent the potentially fatal complications of sickle cell disease during infancy.[4]

Screening for Hemoglobinopathies

As newborn screening programs considered the feasibility of adding hemoglobinopathy testing to their programs, difficult questions arose. Who should be screened? Should screening be universal or targeted and, if screening is targeted, how is the targeted population defined?; What should be done when carrier conditions are identified? That is should traits be reported? Do the clients have a right to know laboratory findings? Do laboratories have the right not to tell the clients? Unfortunately,

some of these questions remain unanswered today. Although the Consensus Statement from the 1987 National Institutes of Health Consensus Development Conference addressed most of these issues, controversy over some of these issues remains in the medical community.

The Texas Newborn Screening Program began in 1965 and sickle cell screening was added to the program in 1983. The program is mandated by state law and screening is done universally, and like most states, specimens are collected from heel sticks onto filter paper. The first specimen is usually collected while the infant is still in the hospital. A second specimen is collected when the infant is seven to fourteen days of age.

When hemoglobinopathy screening began, the analytical method was cellulose acetate electrophoresis combined with citrate agar electrophoresis for confirmation. Patients were retested at age three months for confirmation of the disease. Currently, isoelectric focusing is performed on all specimens. Those samples exhibiting characteristics of disease are confirmed by DNA sequencing within a few days using the same filter paper sample. Isoelectric focusing is preferred to cellulose acetate because the resolution allows differentiation of hemoglobin types not possible with cellulose acetate electrophoresis. It also lends itself to high volume testing, is much easier to read, and is less subject to interferences arising in older samples. DNA confirmation is preferred to citrate agar because of the speed with which specimens can be confirmed. The usual turn-around time is about two weeks.

In Texas, laboratory reports on all patients are returned to the submitter. Laboratory results indicating a disease or carrier status are returned to the submitter with a statement requesting that another test be conducted in three months. Reports indicating a disease are followed by the case management staff in the Bureau of Women and Children. The procedures for case management are as follows: 1) The doctor is contacted by telephone and letter to be sure that follow-up is done. 2) A certified letter is sent to the parents. 3) The nurse or social worker for the area is contacted. If the family does not have a primary care physician, and lives in an area that is not covered by a social worker or nurse, a local public health nurse is used to assist the family in getting into the medical system. 4) If DNA confirmation has not been completed by the time the infant is two months of age, the physician or health care provider is contacted again by letter and asked to send more blood for confirmation. The health care provider or family is contacted at specified intervals until confirmation is completed or the family is lost to follow-up. Once confirmation has been completed and the patient is receiving treatment, the file is put into a recall system and follow-up occurs annually. (Figure 1)

The Texas Newborn Screening Hemoglobinopathy Program has an eighteen-member advisory committee consisting of pediatric hematologists, pediatricians, family practitioners, a genetic counselor, a clinical chemist, and a sickle cell association representative. This group meets once a year to discuss and evaluate the program, look at statistics, advise the staff, and discuss current and recent research findings.

Conclusion

Currently, most states have some type of screening program for sickle cell disease. Although there are still unresolved questions, the evidence clearly supports decreased morbidity and mortality when patients with sickle cell disease are detected in the newborn period. In the Texas program, over 3.5 million infants have been screened for sickle cell disease. Over fourteen hundred infants have been identified with sickle cell disease and are being actively followed.

Analysis of mortality data for the past ten years of the Texas Newborn Screening Hemoglobinopathy Program demonstrates a mortality of 0.8 deaths per 100 person years. This is down from our baseline data of 2.69 deaths per 100 person years during the first five years of the program (Table 1). Use of DNA in the screening laboratory has decreased the time from birth to disease confirmation to an average of approximately three weeks. Research into gene therapy continues to provide hope that, eventually, a curative mechanism will be found to counter the adverse effects of sickle cell disease.

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Figure 1

Table 1

DEATH RATE FOR INFANTS WITH SICKLE CELL DISEASE

YEARS SCREENED	INFANTS WITH SICKLE CELL DISEASE	NUMBER OF YEARS SCREENED	PERSON YEARS
1984	83	10	830
1985	102	9	918
1986	109	8	872
1987	109	7	763
1988	124	6	744
1989	115	5	575
1990	115	4	460
1991	115	3	345
1992	132	2	264
1993	102	1	102
TOTAL	**1,106**	**55**	**5,873**

1. Total infants that expired with sickle cell disease = 48

2. 48 deaths per 5,873 person years

3. 0.8 deaths per 100 person years

Mountain States Regional Genetic Services Network (MSRGSN): Guidelines for Genetic Services

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History

The MSRGSN Finance Committee had, since its inception in 1986, explored methods to optimize funding for genetic services from public sources, including Medicaid, as well as from private third party payers. By 1988, interest in pursuing public health funds for genetic services emerged as the primary concern of the committee, as well as of the Network as a whole, and a needs assessment of genetic services throughout the six state MSRGSN was proposed. In an effort to begin the needs assessment process, identification of unifying values and priorities for use of scarce resources was determined to be necessary and the 'Guidelines for Genetic Services' grew out of this effort. The 'Guidelines' document was developed to inform the needs assessment process of what MSRGSN membership, by collective agreement, felt were necessary components of 'genetic services' as well as to spell out the underlying values and philosophy of the Network membership regarding genetic services.

While this document is intended to assist the MSRGSN members, staff, and committees in focusing on the values and priorities established collectively, it is not intended to be the *only* tool for elaborating these concepts. It was noted early in the process of creating the guidelines that other iterations of this document would be developed by various committees for various audiences. For instance, the Clinical Services Committee is utilizing the guidelines to establish a quality assurance tool, the Education Committee uses the guidelines in developing public education materials, and the Finance Committee is working on a document to be used as an educational tool for health care reform policy makers, legislators, boards of directors of private health insurers, etc. The 'Guidelines' provides consistency and direction for all of these projects and serves as a reminder for the Network of the priorities of the membership.

In the process of developing the guidelines, all committees reviewed and provided input and valuable criticism. Not only were genetic services providers, public health administrators, and laboratory personnel involved in the creation of the 'Guidelines', but consumers of genetic services also had considerable influence. The MSRGSN Consumer Issues Committee, along with the Finance Committee, provided the majority of the work that went into development of the document.

Purpose

The 'Guidelines for Genetic Services' represents the collective values and priorities of the membership of the MSRGSN regarding the provision of genetic services. This document is intended to be used as a guide for *all* committee work and network activities. It is meant to be the basis for all educational materials produced by the various committees as well as the basis for all other work products coming out of the network. It is meant to be the philosophy and values statement from which educational tools can be created. And they are being created.

Uses

This single document has been the impetus for many collaborative projects carried out throughout the Mountain States Region. To mention a few:

1) Needs Assessment

The original idea for the 'Guidelines' was to assist in a region-wide needs assessment. This effort began two years ago with design of a needs assessment tool to identify gaps in genetic services in the region, be they geographic, socioeconomic, condition or community specific, etc. The needs assessment is currently underway, spearheaded by the Clinical Committee and, while needs assessment is never complete, this phase will be completed by the Annual Meeting in August.

2) Cost/Reimbursement Analysis of Genetic Services throughout the MSRGSN

Needs which surfaced while developing the 'Guidelines' were the needs to delineate clearly the cost of genetic services in sites throughout the region, to identify reasons for any dramatic differences in cost from one service site to another, and, finally, to quantify how much of the actual costs were reimbursed. The Finance Committee has undertaken this cost/reimbursement analysis of services throughout the region. Dr. Eva Sujanski has completed the costing piece of the project and will have the reimbursement analysis completed to present at the Annual Meeting this year.

3) Assessment of Needs of Patients' Currently Receiving Genetic Services

The Consumer Issues Committee has vociferously and tenaciously advocated the need to proactively solicit input from families who are the recipients of genetic services. In cooperation with the Finance Committee, this activity is being undertaken. While surveying costs of services, Dr. Sujanski has also developed a mechanism to survey patients' being seen in the genetic service sites throughout the six states which comprise the MSRGSN. The patients who agree to participate are being asked about their level of satisfaction with the service providers, but are also being queried about how they feel about the timing of the services (were they seen early enough, too soon), the helpfulness of the services and the appropriateness of the services. They are also being solicited for input about the form in which they prefer education to occur (e.g., in person counseling, telephone counseling, video-taped materials, written materials, etc.).

4) Spanish-speaking Community SPRANS Grant Activities

The Consumer Issues Committee is collaborating with the Arizona Department of Health to improve genetic services for communities of primarily Spanish-speaking people along the US/Mexico border. The largest 'minority' population throughout the MSRGSN is the

Spanish-language communities. The effort in Arizona to better serve this population will be evaluated and emulated by other providers in the region.

5) Educational Activities

All of the MSRGSN Committees are utilizing the 'Guidelines' in developing educational materials and presentations regarding various aspects of genetics for many different audiences. For example, managed care administrators will be approached using a document being developed by the Clinical Services Committee and the Education Committee which will include the cost analysis data developed by the Finance Committee. This effort is based upon priorities for funding established by the MSRGSN membership and delineated in the 'Guidelines' document.

Summary

Although the development of 'Guidelines for Genetic Services' took considerable time and effort, and, frankly, many of the participants feared the resulting document would only collect dust on a bureaucrat's shelf, it has come to be the seminal, central focus of the membership, and informs all MSRGSN activities. Because it was developed as a full court press collaborative effort among all the network's committees, was reviewed, revised, and finally voted upon by the *entire* membership and because the collaborators included consumers as well as providers of genetic services, it has become a very useful, vital part of the network.

There was a time, a few years ago, when some of us were concerned that perseverance in the cause of creating the 'Guidelines' had become perseveration. However, once the process of defining values and priorities had been accomplished, it was clear that the product was well worth the effort. The 'Guidelines' document is a living, changing entity. It has been through several interactions and will doubtless go through many more as new technologies are developed and utilized; as ethical considerations are more fully delineated; as the genome is further mapped and genetic components of many chronic conditions are identified.

GUIDELINES FOR GENETIC SERVICE DELIVERY

Philosophy

Genetic services shall be available to all persons with concerns about reproductive risks or potential hereditary problems. Services are to be family centered and community based. They shall include but not be limited to the following:

- Affected persons
- Individuals with a family history of problems, including an abnormal child
- Pregnancies exposed to potentially harmful agents
- Pregnancy losses or adverse outcomes
- History of infertility
- Individuals at increased risk because of age or history of chronic health problems, e.g. diabetes, teratogenic exposures

These services shall be available to all regardless of income. Services as provided by certified counselors shall be covered by all health care third party payers including:

- Private insurance
- State/federally funded health insurance/plans
- HMO and other pre-paid health insurance programs. In addition, provision will be made to include counseling for medically indigent persons through a sliding fee scale or free services when necessary.

Genetic services shall be ethnoculturally appropriate and geographically available. In each community there shall be health personnel who have been trained to screen for genetic problems and complete a preliminary examination. There shall be regional clinics staffed by certified personnel. When necessary families will receive assistance with transportation arrangements to a genetic center.

When an evaluation involving laboratory studies, imaging, etc., is recommended and the family of the individual wishes to pursue this, there will be financial resources available. This evaluation may be done in the home community or at the genetic facility and may require a short term hospitalization.

The family shall have access to the results of any evaluation in a form which is meaningful to them. This may include any or all the following:

- Personal sessions with the counselor, repeated as needed
- Written information in the primary language of the client and in terms understandable to the client
- Copies of evaluation and/or study results

The family/individual shall have access to those services needed for the most effective management of the genetic conditions.

- Primary medical care
- Specialty care as needed for treatment or amelioration
- Psychological and/or supportive counseling
- Access to appropriate information and to parent support groups
- Supportive help to assure optimal level of function
- Ongoing financial medical coverage
- Therapy and education for all age groups

When there is an increased reproductive risk, couples shall have access to prenatal diagnosis using state of the art techniques. Reproductive options including abortion for genetic indications shall be available with no financial restrictions or limitations.

Repeat genetic evaluations shall be available as new information or questions arise. This will require a registry which will ensure dissemination of new genetic information.

The Genetic System Requirements

Certain requirements are needed for an effective and efficient genetic service delivery system for families, individuals and children. The system shall include:

- Payment sources such as self pay, Medicare/Medicaid, insurance, HMO's and sliding fee scales
- A genetic community which includes teaching facilities, accredited laboratories, private and public providers
- Information management and regional communal data systems which provide needed outcome and planning information
- Statutory authority to enable agencies to administer genetic programs, e.g. newborn screening
- A system which allows for protection of individual rights regarding reproductive options and protects against discrimination on the basis of a genetic condition
- Sources of referral which include birth defect registries, private obstetricians, pediatricians, family practitioners, public health nurses, community clinics, self referral and other health care providers
- Access to library management information systems to serve as a resource to professionals and families
- A tracking system to provide for follow-up services including individuals at risk for genetic disorders
- A genetic education system which includes professional (undergraduate, graduate and continuing education) patient/family, and general population and public schools
- Advisory group which includes parents and professionals

Personnel Requirements
All clinics and facilities associated with genetic services shall have as a core a physician and counselor who are board eligible or certified by the American College of Medical Genetics.

The above will have access to:

- Physicians, genetic counselors, other health care professionals who are board eligible or certified by the American Board of Genetics
- Laboratories which participate in a regional or national quality assurance program
- Subspecialists in the area of medical genetics, clinical cytogenetics, teratogenetics, clinical and molecular genetics.
- Other health professionals, e.g. registered nurses, medical social workers, registered dieticians

Clinical Requirements
The following elements are the basic components of comprehensive genetic evaluation. Whenever possible a multi-disciplinary team approach shall be utilized.

- A review of all appropriate medical records, psychological evaluations, laboratory values and radiographs
- A family history and a pedigree
- Prenatal history: including length of gestation, maternal weight gain, position, fetal activity, maternal illness, potential teratogenic exposures, and other problems during gestation
- Perinatal history
- A history regarding growth and developmental milestones
- A history of school performance and/or behavioral difficulties
- Other medical history regarding hospitalizations, surgeries, major illnesses
- A complete examination including dysmorphology
- Laboratory studies as appropriate
- Differential diagnoses and treatment plan
- Counsel regarding the diagnosis or differential diagnoses
- When the diagnosis is firm, prognosis, recurrence, histories, prenatal diagnosis and modes of therapy shall be discussed
- Referral to appropriate support services and family support groups
- Reports summarizing the clinic used to be sent to primary care provider, referring source, and the family
- Follow-up visit(s) to discuss the results of the evaluation and to reinforce counselling given including pertinent educational information to the patient and family

In addition to the comprehensive genetic services listed above there are unique age specific genetic services which should be included. Services shall be family centered and community based and be available to patients and families throughout life.

Prenatal
Cytogenetic, biochemical, DNA analysis
Maternal serum AFP screening
Pregnancy options
Targeted ultrasound
Amniocentesis, CVS
Teratology information services

Birth/Infancy
High risk delivery services
Birth/infant screening
Fetal pathology - products of conception, embryonic tissue, stillborn infants, placental analysis
Neuro-developmental evaluations

Childhood
Developmental evaluation

Adolescents/Adulthood
Genetic reproductive counselling
Transition services - medical, vocational, social
Inborn metabolic error management

Follow-up Requirements
Services shall include:

- Patient Education:
  - Age appropriate
  - Ethnocultural related
  - Conveyed in a compassionate manner
  - Offered in a timely fashion
  - Ongoing or available as needed
  - Current

- Primary Care:
  - Comprehensive
  - Accessible
  - financial
  - geographic
  - Provided by qualified personnel

- Specialty Care
  - Multi-disciplinary
  - Condition Specific

Developmental focus
Supportive services-OT/PT
Family centered

- Tracking and referral system: Agencies serving clients and families with genetic related conditions
  EPSDT (Medicaid clients)
  Birth Defects Registry
  Childrens Special Health Services
  Newborn Screening Program
  Handicapped Infants and Toddler Act (99-457)
  Public Health Agencies
  Schools
  Counseling agencies
  Parent support groups
  Adoption agencies - family health information to authorized individuals which is appropriate and confidential

Clinical Genetic Services and their Relevance to Public Health

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Introduction

Medical genetics is the discipline of medicine which deals specifically with hereditary disorders and birth defects. The field is young, having developed only during the last 30 years, and is currently undergoing an explosion of new information through the Human Genome Project, much of which is relevant to large segments of our population. As such, it is changing from a small academic specialty that had little impact on medicine as a whole to one which is central to our understanding of most human disease. Every branch of medicine benefits from gains made in our search to unravel the secrets of inherited disorders and birth defects; understanding even of rare genetic disorders has implications for more common ones. For example, it is now known that cancer is a disease of tissue genes, based in part on the study of rare, inherited cancer syndromes. *Most common diseases result from interaction between genetic factors (genes) and environmental influences.* Unlike most medical and surgical specialists, however, the medical geneticist's area of expertise is not organ-specific, but encompasses a broad array of disease entities overlapping many specialists and extending throughout the life-cycle. This reflects the fact that the broad spectrum of birth defects and genetic disorders may become evident at widely different times of life.

Diagnosing the less common of this panoply of conditions can be difficult, requiring special medical knowledge and unusual tests; explaining the complex etiology, pathogenesis and diagnostic tests to families, even for the more common conditions, is both difficult and time-consuming. Studies have shown that this type of medical care is severely under-compensated; only 25% to 30% of the time spent is actually reimbursed. In the past, most of these services could only be supported in teaching hospitals or similar environments.

Intensive patient education is necessary because of two important aspects of medical genetic conditions: *they can sometimes recur in family members and they can sometimes be diagnosed prior to birth or onset of symptoms.* The information therefore empowers families uniquely to make informed choices that will affect outcome, such as for presymptomatic or prenatal testing. The development of medical genetics has been strongly influenced by the growth of the consumer movement; respect for patient autonomy is one of its guiding principles.

Public Health Relevance

State Departments of Health emphasize prevention of important causes of morbidity and mortality as well as assurance that quality services are available and accessible to all citizens. The resulting service network fostered by public health resources is increasingly referred to as a "Safety Net" for the poor, disadvantaged and multiply handicapped. During the childhood and adolescence of medical genetics as a specialty, public health agencies have been important supporters of its growth and

development, because of its perceived value to all citizens. Medical genetics is now approaching its maturity as a branch of medical care, paradoxically at a time when all special (and expensive) medical services are undergoing increased scrutiny as to their relevance to general healthcare. Rather than separating from its public health association, we believe the links between public health and medical genetics should be strengthened, for the following reasons:

- The new research proves that many of the most important biological causes of morbidity and mortality are genetic. Virtually everyone is touched by the health effects of some variation in one of their genes at some time in their life.

- Early testing, appropriate diagnosis and treatment may improve outcome, by primary or secondary prevention.

- Keeping up with the rapid increase in knowledge in genetics is increasingly difficult; some new discoveries will have far-reaching public health implications, necessitating regular exchange of expertise between medical genetics and public health professionals for optimal application to the population's health.

- Individual services are still labor-intensive and poorly reimbursed; maintenance of access for all families therefore still requires assistance. As the number of valuable tests and options for families increases, the costs are not decreasing.

- Genetic services can guide both healthcare providers and patients through the confusing maze of rare diseases and incomprehensible tests; for some, medical genetic services will mean their only access to unique diagnostic tests and new treatment services, to hard-to-find information about rare diseases and to patient support groups centered on uncommon conditions.

We believe that access to genetic services serves the public good by providing citizens and their healthcare providers the knowledge prerequisite for decision-making which can affect and possibly improve their own health and that of their families.

Preventive Activities and Medical Genetics

Specific prevention activities of any healthcare field are of obvious interest to a public health plan. The preventive aspects of genetic services as a whole are difficult to quantitate and largely uncalculated. Moreover, the natural history of many genetic disorders is inadequately documented in medical literature and poorly understood, increasing the difficulty of documenting their value through measurable outcomes. In addition, since birth defects and genetic disorders are inborn, the division of "primary" and "secondary" prevention activities require interpretation in this light.

Primary Prevention

Primary prevention usually refers to prevention of the morbidity of disease before it happens and to the prevention of mortality from disease. The current state-of-the-art in prenatal primary prevention

has developed through close collaboration between both obstetrical and genetic professionals. Medical geneticists have been instrumental in the development of specific prenatal diagnostic tests and in the refinement of prenatal syndrome diagnosis using a variety of test modalities. The major role of genetics in primary prevention has been in the education of families regarding their risks to have children affected with birth defects or genetic disorders and in the mechanisms to reduce that risk, through the process of genetic counseling, as follows:

- Prevention of the occurrence of birth defects in those at increased risk, through the use of folic acid, periconceptional vitamins and prenatal care; genetic professionals also provide counseling as to avoidance of alcohol, risk/benefit ratio of anticonvulsants and other maternal medications and the benefits of optimal management of maternal diabetes.

- Early prenatal identification of fetal anomalies in which prenatal intervention may prove life-saving to the fetus; genetic counseling as to prognosis, possible etiologies and options for prenatal management are integral to family decision-making.

- Preconceptional genetic counseling of the family at risk for hereditary conditions to allow autonomy in family planning; at times, this requires sophisticated diagnostic assessment of the affected family member(s).

Past references to prenatal testing for genetic conditions and subsequent termination of affected pregnancies as a form of primary prevention have cast an unwanted negative impression on the value of prenatal diagnosis. This belies the great success of prenatal diagnosis in encouraging families fearful of hereditary conditions to have healthy babies, who outnumber those found to be affected many times over.

Postnatal primary prevention has been accomplished through:

- Newborn biochemical screening programs for inborn errors of metabolism, with treatment programs to prevent morbidity and undesired outcomes such as mental retardation.

- Prenatal diagnosis of genetic conditions in families at risk for certain inborn errors of metabolism with prospective treatment from birth.

Secondary Prevention

Secondary prevention refers to prevention of future morbidity in those already identified as having a condition or disease. This is the area where medical genetics most clearly functions as a specialty of medicine but also where it assists the "Safety Net" of services for the disadvantaged. Knowledge of the common and rare birth defect and genetic conditions is a prerequisite to provide appropriate preventive and palliative care to affected individuals and their families. Many families embark on a diagnostic odyssey until they encounter a professional skilled in the diagnosis of these low incidence conditions; diagnosis is occasionally made even more difficult by the tendency of some inborn errors

of metabolism to mimic common diseases. Misdiagnosis can lead to unnecessary tests, increased costs (medical morbidity, psychological sequelae and increased financial risk) and even to unnecessary operations. Failure to diagnose or misdiagnosis can also lead to serious, life-threatening, preventable complications. Because some conditions can be identified in a presymptomatic or early state, preventative and anticipatory medical care can also prevent onset of complications in some affected individuals. Medical genetic services therefore provide:

- Early clinical recognition and diagnosis of rare birth defects and hereditary conditions, with prevention of secondary pathology and morbidity and early referral to appropriate treatment.

- Education and assistance in the proper use, ordering and interpretation of complex, expensive genetic diagnostic tests, resulting in reduction of healthcare costs through appropriate usage.

- Education of family and medical providers as to natural history, appropriate anticipatory management, prognosis, educational resources and hereditary basis; assistance of primarycare providers in management of their affected patients to plan the most cost-effective long term management.

- Recognition of the complications of rare diseases and prevention of morbidity and mortality arising from missed diagnoses; consultative assistance to other healthcare providers in dealing with unfamiliar disorders and their often complex complications.

- Assistance in the multi-disciplinary treatment teams for complex congenital disorders, such as craniofacial disorders, neurocutaneous disorders, connective tissue disorders, hemoglobinopathies and many others.

- Expertise in the diagnosis and management of many orphan diseases (disorders present in very few individuals), most especially the inborn errors of metabolism, which appear to be within no other specific specialty area of medicine.

Surveillance

Prevention activities require a frame of reference. Many states monitor the occurrence of birth defects, spontaneous abortions or other similar information. Neonatal and perinatal morbidity and mortality are also monitored. Birth defects are the second most prevalent specific cause of perinatal mortality, after "conditions arising in the perinatal period". medical genetics can assist surveillance activities by offering expertise on:

- Diagnosis of birth defects, isolated as well as syndromic

- Assisting analysis of potential and known teratogens

Recommendations

The State Department of Health should maintain its strong record of leadership in monitoring, prevention and treatment of birth defects and inherited disorders by maintenance of a program with the following components:

- An identifiable unit devoted to birth defects and genetic disorders with a designated coordinator
- Newborn biochemical screening program with diagnostic laboratory and follow-up program
- Birth Defects Registry
- Teratogen database and referral system
- Database of genetic and other services available with a system to assure availability and access to quality care
- Commitment to comprehensive care for multiply handicapped, special needs and disadvantaged and/or vulnerable infants, children and adolescents
- Linkage to a system to assist transition of adolescents with birth defects and genetic disorders to a system for adult care, including linkages to Developmental Disabilities Services and other services for handicapped adults

In addition, leadership will be required to maintain the gains in care for families with birth defects and genetic disorders which have occurred over the last thirty years and to maintain access to the improvements in healthcare which will result from the new knowledge increasingly being developed in this field. This must occur in the face of changes in the healthcare system which discourage specialty care in the understandable desire to reduce medical costs.

Issues specific to medical genetic services which should be pursued include the following:

- Codification of the role of genetic counselors as bona fide mid-level health practitioners. Whether this will encompass licensure should be explored as to feasibility and appropriateness. Regulation may be required to compel health insurers to reimburse genetic counseling services as distinct from physician medical genetic services. Insurers may be more accepting if they are made aware that genetic counselors facilitate informed consent, support consumer empowerment and contribute positively to patient satisfaction.
- While prenatal genetic services may become increasingly available as a part of prenatal care, diagnostic medical genetic services will require special attention in order to maintain their accessibility and availability to families with lesser financial means. Designation of "centers

of excellence", financial subsidy and maintenance of high clinical standards should all be considered as mechanisms to keep these services available and accessible.

- Efforts should be made to ensure that medical genetic services are available and accessible through managed healthcare policies, and are considered part of the routine medical coverage of all plans providing specialty medical care. Plans should be encouraged to pay for unusual genetic tests at specialty research laboratories, given appropriate genetic indications. At minimum, these recommendations should apply to state-sponsored Medicaid managed care contracts.

- Optimally, medical genetic services should link to the treatment services available for families with birth defects and genetic disorders. However, this is increasingly difficult when dealing with managed care financing arrangements because of their tendency to parcel out each different type of service, possibly to providers at different locations. Managed care plans should be encouraged to use comprehensive multi-specialty centers of excellence to provide coordinated care by qualified specialists for those with complex medical needs.

- The future role of medical genetics will expand to include many conditions common among adults, such as cancer and neurodegenerative diseases. Given the wide-spread media coverage of genetic tests and the public's concern about possible usage of these tests both to their benefit and their personal harm, strong consideration should be given to the creation of a Genetics Advisory Group which can assist policy development and technology assessment in Departments of Health, Insurance, Human Services and any other section of state government which needs to address issues related to genetics.

Impact of Medicaid Managed Care on Implementation of Genetic Services Guidelines: The Tennessee Experience

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Introduction

At midnight on January 1, 1994, TennCare, Tennessee's experiment in managing Medicaid costs, began. A little over two years later, some observations can be made regarding its effects on the Tennessee Genetic Centers' ability to continue delivering genetic services. Tennessee's Department of Health (TDH) had implemented a statewide genetic service delivery program in the 1980's, but this was prior to the rapid health care delivery changes. This experience should be considered by states not only anticipating changing or adopting genetic service guidelines, but also if Medicaid changes are expected. Genetic Centers and states should strongly consider making genetic services part of a state's Medicaid plan before conversion to a variety of MCO/HMO/PPO plans.

Background

Tennessee (TN) has two major pieces of legislation regarding genetic services: a 1963 statute mandating newborn screening for Phenylketonuria (PKU); and an annotated law passed in 1985 mandating both newborn screening for selected metabolic disorders, and 'genetic testing' (genetic services). The specifics of implementation and standards were included in the "Rules and Regulations" of TDH, which is now being updated (Genetics Advisory Council, 1996). The TN revised guidelines predate the state genetic service guidelines being proposed by the Council of Regional Networks (CORN, see elsewhere this publication), and include: goals (purpose, availability, and access to genetic services); definitions; composition of a genetics advisory council; scope of services; standards of genetic professional staff; monitoring of Genetic Centers; data collection; and newborn screening regulations.

Tennessee's demographics are listed in Table 1. In the early 1980's, when the original federal genetic service funds for Tennessee were not renewed, the state assumed the costs (slightly less than $500,000). To provide the TDH with both a needs assessment and goals for future genetic services, an outside review was solicited, and this revealed:

- six separate, but unequal, Genetic Centers in existence;
- inadequate funding; and
- need for further statewide services

Recommendations included:

- stratification of Genetic Centers (comprehensive, on-site, or satellite levels);
- provision of genetic services statewide; and

- careful planning and gradual phase-in of a major funding increase (recommended increase to $3 million within 5 years)

Since 1985, the following have been implemented:

- genetic services program legislation passed;
- genetic service guidelines developed, as regulated by TDH (defined availability and scope of genetic services);
- Genetic Advisory Committee established (representation from each qualified Genetic Center, TDH, Consumer/At Large);
- newborn screening protocols defined; and
- standards for evaluation of Genetic and Sickle Cell Centers developed

The goals in the legislation and guidelines were to:

- decrease morbidity/mortality associated with genetic disorders;
- provide genetic services and increase cooperation among the regional Genetic Centers, regional Sickle Cell Centers, and newborn screening follow-up treatment centers;
- make services available to any TN citizen who is diagnosed with or *at risk for* a genetic disorder *regardless of ability to pay*;
- provide newborn screening for selected disorders through the state laboratory *and Regional Network Laboratories* to clarify/confirm abnormal newborn screening and other tests, *as available*;
- provide diagnostic evaluation, genetic counseling, and education services;
- provide professional education/training in medical genetics;
- provide public health education regarding availability of services;
- collect data from Genetic and Sickle Cell Center activity; and
- consult/refer to centers in the genetics network

In the intervening 10 years, the health care delivery services have changed considerably, driven largely by the increasing percentage of the GNP occupied by the health care dollar. Programs have arisen rapidly as experimental solutions to the economic health care problem. While programs vary considerably, most share in common:

- emphasis on primary medical and preventive care
- negotiated competitive capped contracts for specialty and laboratory services; and
- application of 'business models' to health care delivery

During this same time the Genetic Centers increased Medical Geneticist and Cytogeneticist positions (3x); certified Genetic Counselors (5) filled a previous void; Molecular labs and Molecular Geneticists grew from none to 3; Cytogenetic and Inborn Errors of Metabolism (IEM) labs remained constant; and an additional Genetic Center was created. These increases came largely at the cost of the

academic medical center funds, not state funds. Newborn screening began for Sickle Cell anemia and Galactosemia. Sickle Cell Centers, which previously were locally handled *ad hoc*, became organized with the formation of two comprehensive and four satellite centers. In addition, a birth defects registry was begun, separate from the Genetic Centers, whose goal was to identify epidemiological data (teratogen, genetic, and geographic factors), identify service needs, and address issues for future planning and coordination, evaluation, and education.

The Genetic Centers' allocation has remained under the same total funding of dollars since 1990. Allocation of dollars is granted primarily by a pre-agreed upon formula, with new patients, lab testing, and 'core' costs comprising 80%. Extra credit is given for outreach as incentive for centers to provide service to more rural areas. Problems with the formula include: 1) centers compete for fixed dollars causing competition and suspicion among centers; and 2) new patient and laboratory testing efforts are heavily rewarded, at the expense of follow-up visits. The Genetic Centers personnel/staff have remained remarkably stable over the past decade, but the state hierarchy in TDH-Maternal and Child Health (MCH), and specifically the Genetics/Newborn Screening section, has undergone multiple administrative organizational, as well as personnel, changes. This necessitated a reeducation of state personnel regarding genetics, genetic services, and needs of the Genetics Units.
Therefore, proactive handling of genetic and economic issues has been difficult. However, while attempts were made by the legislature to reduce the funding, data supplied by the Genetic Centers was used for aggressive persuasion by the Director of MCH to retain the funding at the same absolute dollars. Since funds are not available for salary increases, funding has actually decreased.

By 1994, TN statistics collected from CORN data submitted by the Genetics and Sickle Cell Centers revealed the Genetic Centers rendered service to TN residents with over 2500 new visits/consults; 1800 follow-up visits; 5700 prenatal visits; and 500 outreach visits. Approximately 3000 professionals/public individuals (medical students not included) received education. Sickle Cell Centers provided over 1000 clinic visits and 5000 follow-up contracts, while 3500 individuals received education. Racial distribution revealed TN genetic clients to be primary Caucasian (81%) with African-American making up 17% (the latter make up 92% of the Sickle Cell Center clients). Ethnic distribution revealed 5% Hispanic population. Clients also were primarily urban (almost 60%). About 15% of genetic patients were out-of-state residents as most of the major Genetic and Sickle Cell Centers are near one or more of the eight states that border TN (see Table 1).

TennCare

TennCare began in 1994. The state turned over the funds for medical management to 18 MCO/PPO organizations to provide services to the Medicaid-eligible population after only *eight months* of planning and by executive order (Table 2), with no guidelines, and with formal approval from Health Care Financing Administration for TN to initiate the program less than 2 months before its inception. The lack of requirement of state legislation resulted in much of the information remaining in the hands of the financial administration, and thus very few details were made available to the public. The medical community, either organized or individually, generally received their information through the press. Of the eighteen organizations initially formed to provide medical coverage for the Medicaid

eligibles, only twelve remained by the time TennCare began. When Medicaid eligibles were balloted to chose their MCO/PPO plans, only about 50% responded. This occurred apparently because of both the lack of information about the programs, the newness of the health plans, and the lack of knowing with which plan a particular primary care provider (PCP), specialist, or hospital would sign up to provide services. The Academic Medical Center (AMC) plans expected about 50% eligibles, but only 10-30% enrolled. Their population was generally sicker and more costly (e.g. complex illnesses, requiring specialized care), resulting in adverse selection.

When about 50% of eligibles did not respond to ballots for choosing their preferred MCO/PPO, the state assigned the remaining eligibles *based upon the previously selected percentages*. However, these selections were based on non-regulated advertising and enrollment practices. The latter included some plans enrolling prisoners (handled under another state plan), and promising 'perks' for enrolling in their plans. Charges of fraudulent practices were made by other MCO/PPOs. The uninsured were not allowed to participate until after January, 1994.

Major problems developed with TennCare, as was anticipated by its speed of implementation (Table 3). One state financial administrator's response to the speed and lack of medical input was that they could either work out all the problems ahead of time and start later, or start immediately and let the problems work themselves out as they went along. The latter course was much 'less expensive' and that's the way they decided to go. There was no medical input into planning the TennCare model. It is unclear who was responsible for the drafting of the state requirements of the MCO/PPOs to follow so they might receive state funds for operation.

There is no question that for the first 6 months of the program, that PCPs, specialists (genetics included), and hospitals continued to provide care for all the enrollees regardless of plan or referral pattern, so that clinical (genetic) services would not be interrupted. However, this was at financial risk, as without authorized referrals, payment was certainly not assured. Contracts between the hospitals or providers and the MCO/PPOs to provide service to enrollees were *not* in place in the early months. Referral guidelines were being developed by the MCO/PPOs during this time, and, until they were clarified and communicated to the hospitals or providers, chaos ruled. Providers continued to supply the health care. While, in many cases, approval was given retroactively, revenue was lost irrevocably from seeing patients on a compassionate basis without referrals. The lack of a phase-in period or pilot projects greatly hampered the ability of the state, the MCO/PPOs, hospitals, and providers to provide medical care to enrollees. Anecdotally, it was perceived that in the early phases of TennCare, patients had a higher acuity level (delayed seeking medical care, sicker when they got to point of care).

In November, the state elected a new governor/administration who promised to rectify TennCare problems. They were in office for only a month when cost overruns from the previous administration of over $200 million were announced. One of the many results of this discovery was the pulling of over $30 million in state Graduate Medical Education (GME) funds. While these have mostly been restored through a system of direct negotiations with the medical schools/centers, the impact both

locally on the reduction in GME primary care training positions and nationwide perception of GME training in TN was dramatic.

Specifically, the TennCare effect on Genetic Centers is seen in Table 4. There are three areas to consider: the genetic clients served, the genetic state liaison personnel, and the genetics units themselves. Referrals dropped initially, but have gradually increased. Genetics Centers provided care to many clients without referrals during this time as a good faith measure, which was costly. Sickle Cell disease and IEM chronic disease patients who needed to be seen on a regular basis were seen without referrals to continue care until they were identified and examined by a PCP. Clients assigned to MCOs were, and still are, slow to obtain written approval from their PCP as a 'gatekeeper' prior to seeing the geneticist. Currently specialists are still unfamiliar with having to first make recommendations to the PCP for referral to other proviers, especially with patients requiring multiple specialities. Furthermore, IEM metabolic patients (PKU, etc.), may need a separate approved referral for different providers on an IEM-metabolic team, such as Medical Geneticist, Nutritionist, Psychologist, laboratory services, etc. depending on the institution of billing for each. Also, rare and unusual medication and medical foods, required for many metabolic patients on special prescribed medical diets, were initially denied by all MCO/PPOs. This denial puts the patients' health at risk and required costly (in professional time) verbal/written justifications to multiple ancillary providers.

The state's TDH personnel lacked information with which to guide the Genetic Centers. Additionally, they were pulled from their usual duties to support TennCare fully by answering the TennCare 'hotline'. Since the state financial administration did not consult with TDH in designing TennCare, TDH was not a resource for information, and was as frustrated as the providers with the system. However, being state employees, their allegiance was expected.

The Genetics Units were affected, as were other specialties. The greatest casualty was the amount of extra professional time spent on: phone calls (clients, providers, hospitals, health care personnel); paper work (requesting/obtaining referrals); counseling clients regarding the perceived details of the program; documenting improper procedures; answering providers' genetic questions to 'prevent' a referral; coordinating approvals for medication/prescribed medical foods; and obtaining approval for laboratory coverage for genetic tests. This time was given by the Medical Geneticists, Genetic Counselors, Nurses, professional staff, clerical staff, and laboratory technical staff. The Genetic Centers received mixed signals from the state: on the one hand the state, with TennCare, was opting out of administering Medicaid health care and turning this over to approved MCO/PPOs; on the other hand, TDH had set up an extensive system of genetic guidelines and expectations of the Genetic Centers to provide genetic services. These guidelines may now be in contradiction to the policies and practices of the MCO/PPOs. The state wants increased outreach and provision of services, but TennCare supports allowing the MCO/PPO to determine extent of care. Therefore, TDH genetic service guidelines may have to be revised, taking into consideration the MCO/PPO TennCare model. Certain services that are not covered by the MCO/PPO (or by their contracted labs) such as newer molecular diagnostic tests, and certain FISH cytogenetic tests may not be covered by the MCO,

requiring the genetics unit to subsidize the service or deny service to the client, which is in opposition to the TDH state guidelines to the Genetic Centers.

An additional consequence of TennCare, and the managed care approach in general, is that there is the potential for a less than collegial relationship developing between the Medical Geneticist, as a member of the group of specialists, and the PCP. As most Genetic Centers are located in graduate medical education centers, for years the geneticist has provided *ad hoc* information to the PCPs, usually with referrals following. The PCP may prefer to 'handle' a patient and not refer if some guiding information is given by the specialist. This is not chargeable by the specialist. However, the medical center specialist has long regarded his/her role in continuing education for the PCP as an important way to communicate changing medical practices. It is likely that this education will continue in a more formal way (seminars, CME), and the specialist may need to refrain from phone advice on any particular patient, based on medical-legal reasons. There will now be an even greater need for continuing education of the PCP by the Medical Geneticist in a variety of ways (didactic, newsletter, increased communication on specific patients).

Funding for genetic services under the allocation formula has not changed under TennCare, as the two programs are distinct. Reimbursement for TennCare patients dropped to as low as *20%* of charges during the initial phases for some plans. TennCare patients comprise at least 50-75% of the total patients seen in the Genetics Centers, resulting in a dramatic effect on funding. One recent summary from a large AMC pediatrics department shows with Pediatrics and Neonatology combined, collections as a percent of charges were 58% in FY91-92, 50.5% in FY93-94, and 50.2% in FY94-95, considering primary care and specialty care, and including all sources of payment. One sample specialty showed percent of charges from: commercial sources (private, commercial, capped, etc.) of between 60-88%; TennCare plans of between 37-52%. Similar recoveries for specialty care from two surrounding states' Medicaid programs were 40% and 33%. TennCare compares unfavorably with about 55-60% overall recovery from the previous Tennessee Medicaid plan.

Laboratory reimbursement was affected, not only because of very low rates, but also because one major statewide plan contracted with a national laboratory to provide *all* of their out-patient testing at a capped rate. The impact of this on the Genetic Centers varies. At least two of the centers have their clinics within the confines of the academic medical center hospital, and therefore are exempt from this 'outpatient' requirement. One center is a separate fiscal and physical entity from the Department of Pediatrics and must subsidize the laboratory tests for which reimbursements either don't cover or inadequately cover costs. Another choice is not to provide accepted current genetic services, or spend time trying to get 'out-of-plan' approval, which does not guarantee payment. Another center operates a clinic outside the boundaries of the hospital, but is a fiscal part of the Department of Pediatrics. This medical center's laboratories generally refer their genetic specimens to the Genetic Centers labs. The MCO contract judges this clinic an 'outpatient' facility, and all of this MCO's clients have to travel a mile to another laboratory 'draw' site to get any laboratory tests drawn (tests performed out of city and genetic tests are all out of state). Revenue is lost, both from a decrease in specimens, as well as from a decrease in the numbers in the state allocation effort.

Specimens are lost to the nationally run, non-state regulated testing facilities when they are part of a negotiated capped contract with the MCO/PPOs. One full service cytogenetic laboratory has been closed, based partly on TennCare effects. Another problem is loss of local access to specimens. At one comprehensive Sickle Cell Center, blood smears cannot be reviewed by the hematologist at the clinic on patients whose MCO contracts with a national laboratory.

While there are many rules and regulations for all insurance companies, dealing with one Medicaid entity (for between 50-75% of patients) and its rules and regulations is far preferable to dealing with five or six different Medicaid-MCO/PPOs (the usual number available in the major medical center areas).

There have been some positive effects of the establishment of TennCare (Table 6), but none override the problems created primarily by the speed with which the plan, or lack thereof, was implemented. The state's growth in Medicaid spending was reported as increasing at about 20%/year; reportedly under the first year of TennCare, the financial growth increased by only 2%. While this is a truly remarkable savings, the cost borne by the providers in extra, non-reimbursed hours, and low reimbursements, as well as unannotated mortality and morbidity, were not known to be factored into the equation.

State Genetic Guidelines: Tennessee and CORN

In considering both the experience with a one state's Genetic Service guidelines as well as TennCare, the following suggestions are made to any state considering adopting or revising genetic service guidelines (Table 7). Genetic service guidelines do not mean those same guidelines will be part of the state requirements for developing an alternative Medicaid system for their state. Any state requirements for the MCO/PPOs of that state to provide *and* finance genetic services (clinical, laboratory, nutritional, medication, medical food, etc.) will need to be mandated separately. Unless this is done, the MCO may determine who is eligible for, and allowed to receive, genetic services under their own guidelines. Thus, the MCO, not the state or Genetic Center, will control the *availability, access,* and *quality* of genetic clinical and laboratory services for their enrollees. While a geneticist may recommend a particular evaluation, it will be up to the provider to pre-authorize that test. In addition, in plans with capped laboratory testing contracts, neither the PCP nor the specialist may be able to override the MCO's 'law' regarding out-of-plan testing, unless it is an emergency or the patient is hospitalized. (Some hospitals are also beginning to contract capped services with national laboratories.) Therefore, when Genetic Centers and states jointly develop state genetic guidelines, they must remember that these are not the same state regulations that mandate requirements of Medicaid managed-care organizations. Thus, *control over genetic services* may be abdicated to the MCO organization - not the state, the geneticist, the patient, or the PCP. State regulations governing the MCOs may effectively enforce genetic service guidelines, if the state health department has the opportunity to have input into those regulations.

A special note must be made regarding putting Genetic Centers at risk because of state subsidization. The TN genetic service guidelines state that a center will provide genetic service '...regardless of

ability to pay...'. This should be treated with caution. One interpretation is that the state itself sets guidelines for 'ability to pay'. Therefore if one is 'self-pay', then they do not qualify for state Medicaid, SSI, or Children's Special Services subsidization. The state has determined that they can 'pay' for their services. Since TennCare has closed their enrollment for almost a year to the uninsured, attempting to cover the uninsured by a state may be a worthy but difficult to attain goal. Better phrasing might be that the Genetic Center should accept clients *regardless of source of payment*. The state should not use language that could be interpreted as meaning genetic clients will not be charged nor should an MCO be able to argue that because of Genetic Center state funds, that all services and tests are 'free'.

Conclusion

The changing scene of funding for health care services will bring several experiments, such as TennCare, up for consideration by states eager to establish their own cost-saving plans. It is a time that Genetic Centers within a state should be communicating with each other as well as with their state health departments to define the state's interest in genetic services as a preventive tool in health care delivery. Whatever the content of state genetic service guidelines that are adopted, they should pay very close attention to the continued and adequate care for not only genetic patients, but also for the children and clients who require chronic, specialized care. Since the state is administering and determining regulations under which Medicaid MCO/PPOs will receive funds, they are in an excellent position to mandate certain requirements of those organizations both prior to and during their program implementation. Otherwise, both the Genetic Center and the state relinquish control over the access to, availability of, and quality of genetic services provided to the Medicaid-eligible clients in that state. This would not be helpful in reaching the goals of making genetic services available to clients in need of such services.

Table 1

STATE OF TENNESSEE: DEMOGRAPHICS	
Population:	4.6 million
Area:	432 X 119 miles
States bordering:	8 (AR, KY, VA, NC, GA, AL, MS, MO)
Birth/yr. (95):	73,000
Caucasian:	84%
Non-Caucasian:	16% (60% in 6 counties of W. TN)
Urban:	60%
Medical Schools:	4 (UT-Memphis, Vanderbilt, Meharry, E. Tennessee, State U)
Academic Medical Centers:	6 (UT-M, UT-Knoxville, UT-Chattanooga, Vanderbilt, Meharry, ETSU)
Medical Genetic Centers:	6*

*One undergoing changes

Table 2

SUMMARY: CHRONOLOGY OF TENNCARE CREATION	
1993 Spring	Internal state proposals (financial administration, non-medical; no legislation required)
June	TN submits Medicaid waiver request to HCFA TennCare goals: to cover 1.775 million eligibles (1993 Medicaid eligibles plus uninsured)
July	Goals revised down to 1.5 million 18 MCO/PPO organizations 'formed' (2 statewide; rest regional) Academic medical center (AMC) from organizations State responds to HCFA queries
October	Ballots mailed to Medicaid eligibles to select their MCO/PPO Massive advertising campaigns to attract eligibles/uninsured by MCO/PPO; no regulation Little available information for *providers* to choose in which MCO/PPO to participate; nor for *eligibles* to choose the MCO/PPO which their current doctor would be in
November	Only 52% eligibles respond to ballots State *assigns* eligibles to MCO/PPO (based on % of previous selection, although fraudulent and unregulated) Selection unchangeable until 10/94 (open enrollment) HCFA waiver approved (against internal HHS veto)
1994 Jan. 1	TennCare takes effect 12 MCO/PPOs begin Open enrollment
Jan.-Oct.	750,000 Medicaid enrollees - 325,000 uninsured Request to HCFA to move 370 million into programs not covered by contracts
November	New administration elected, promising to solve problems

Table 3

TENNCARE PROBLEMS	
1993	● Executive order created; no legislation required ● No medical input into plan ● Inexperienced organizations formed hastily ● Little information known to providers from MCO/PPO organizations or TDH administrators ● TN had relatively little experience with managed care ● Clients didn't know which organization to choose until their doctor chose ● Little understanding among Medicaid population of managed care ● Fraud and abuse reported (ad strategies, enrollment techniques) ● No pilot projects ● Providers not signed onto MCO/PPO organizations (decreased fees, lack of information) ● AMCs only got 10-20% enrollees
1994	● No gradual phase-in ● No contracts signed at inception of TennCare ● Mass confusion among clients, hospitals, providers ● AMCs had adverse selection
1995	● Cost overruns from 1994 made public ($200 million) ● Graduate Medical Education funds (Medicaid portion) pulled (30 million)

Table 4

TENNCARE: EFFECTS ON GENETIC SERVICE CENTERS

Effects upon: **Genetic clients -**

- Referrals initially dropped, then gradually stabilized
- Medical Geneticist initially provided care without referrals
- Need for multiple but separate referrals for all genetic services (e.g., IEM patients)
- Need for uninterrupted care for the chronic patient regardless of MCO/PPO or PCP (e.g. Sickle Cell disease, PKU, etc.)
- PCPs and specialists not available in certain geographic areas
- Problems in continuing medication or medical foods
- Decrease in patient hospitalization in medical center areas

Effects upon: **State genetic service liaison personnel -**

- Required to support what state mandated
- Professional state health employee's required to work on and support TennCare requirements
- Lack of substantive information on TennCare guidelines from TDH

Effects upon: **Genetics unit -**

- Massive increase in profesional time
- Mixed signals from separate state programs (TennCare vs. TDH)
- Certain genetic services not covered by MCO
- Increased time traveling to non-medical center cites
- Decreased collegial relationship between primary care providers and Medical Geneticist

Table 5

TENNCARE EFFECTS: FUNDING
● No additional state funds for genetic services ● No mandated genetic services care ● Clinical services reimbursement decreased ● Laboratory services reimbursement decreased overall ● Reimbursements >3-6 months in arrears ● Specific centers services affected ● Adjustment to rules and regulations of 6 (per region) MCO/PPOs (instead of one, Medicaid) ● Indirectly decreased Genetic Fellowship funding

Table 6

TENNCARE EFFECTS: POSITIVE OUTCOMES
● Medical foods for PKU, all ages, mandated
● 'Early education' into MCO/PPO language/practice
● Genetic Centers initiated alternative strategies
● Primary care dollars increased to medical centers
● Increased genetic education initiatives to PCP
● Variable changes in hospital lab referrals
● Provision of genetic services to uninsured
● AMCs show promising data of controlling costs
● State Medicaid growth dropped supposedly from 20% to 2% during 1994

Table 7

PROPOSED CORN GUIDELINES: ANTICIPATED EFFECTS ON TENNCARE EXPERIENCE
• MCO, not state or Genetic Center, controls *availability* and *access* by limiting referral pattern
• Reimbursement for genetic services by MCO/PPOs not currently mandated by state
• MCO controls *extent* and *quality* of laboratory services, not state or Genetic Center

National Guidelines for Genetic Counselors: The Drafting of Practice Guidelines by the National Society of Genetic Counselors

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With over a thousand members, the National Society of Genetic Counselors (NSGC) represents a sizeable proportion of the roughly 1400 genetic counselors in the U.S., of whom about 850 are certified by the American Board of Medical Genetics (ABMG) or the American Board of Genetic Counselors (ABGC). Though these numbers appear large to those who recall the early days of the genetic counseling profession, they are minuscule in comparison with the ranks of most health care professionals. Many health care professionals, especially those outside the traditional realms of pediatrics and obstetrics, are unfamiliar with the basic tenets of genetic counseling as defined by the American Society of Human Genetics (ASHG). As the availability of genetic screening and genetic testing grows, and as its reach extends into the more common medical complaints of the adult population, increasing numbers of health care professionals engage in genetic counseling with varying degrees of skill and success.

As a case in point, I recently spoke with a woman who accompanied one of my clients to a prenatal diagnostic session. This friend of my client told me she had genetic counseling during a previous pregnancy and "it was wrong." She then related that her doctor had told her a blood test showed her baby would have Down syndrome, and she had two weeks to decide whether she wanted an abortion. She kept the pregnancy and the baby was fine.

Now, I'm perfectly willing to believe her doctor said nothing of the sort. Most likely the physician told her the blood test showed a chance for Down syndrome and she had two weeks to decide whether she wanted an amniocentesis. In either event, the wrong message was received by a woman who was tremendously anxious for the remainder of her pregnancy and who is now deeply suspicious of genetic counseling. If such miscommunication can occur with a physician routinely exposed to genetic screening tests, what might we expect when other health care professionals and para-professionals undertake to provide genetic counseling?

Though the NSGC does not believe only classically trained genetic professionals can deliver appropriate genetic counseling, it is committed to the principle that all individuals experiencing or at risk for genetic disorders should be able to obtain competent, appropriate genetic services in a timely fashion without inordinate personal cost (*c.f.*, NSGC position statement, Access to Care, 1991). The challenge of making this possible in terms of the public health care mantra (availability, accessibility, acceptability, accountability, etc.) falls in large part to the Council of Regional Networks for Genetic Services (CORN) and to the states. The challenge of developing and maintaining professional standards, credentials, and practice guidelines is properly within the purview of the various professional boards and societies.

The American Board of Genetic Counselors (ABGC) is now the certifying body for masters-level genetic counselors and their training programs. As a trade organization the NSGC does not certify, license or discipline its members, nor can it directly influence the professional practices of others. Its scope includes member education, public education, promulgation of position statements and resolutions, development of practice tools such as codes of ethics, and advancement of the best interests of the profession.

Full membership in the NSGC is currently extended to board-certified genetic counselors; Master's or Ph.D. graduates of genetic counseling training programs; Master's or Ph.D. graduates in such related fields as nursing, social work and public health with three years' experience in genetic counseling. D.D.S. and M.D. trained individuals may be associate members. (NSGC By-Laws, adopted 1979). ISONG, the International Society of Nurse Geneticists, shares a significant overlap of membership and interest with the NSGC, as do the ASHG and the ACMG.

The mission of the NSGC is to be the leading voice, authority, and advocate for the genetic counseling profession. Its members are keenly interested in maintaining high standards of practice and they are ever mindful that inept "genetic counseling" delivered by an unprepared individual can seriously mar the public image of professional genetic counselors as well as do a grave disservice to the client.

Practice Guidelines

Aware of the trend towards written practice guidelines, treatment protocols, and care pathways as tools for professional training, quality assurance, patient education, and reimbursement, we have concluded it is incumbent upon the NSGC to articulate what classically trained genetic counselors do during a counseling encounter, and why we do it in the stylized, distinctive fashion which has evolved over the past four decades. We believe this process has the potential to illustrate the complexity of counseling encounters, create a stronger sense of unity among counselors, enhance our practice performance, improve our standing with employers and referral sources, increase the likelihood of appropriate reimbursement, and educate the public in general and our clients in particular.

The debate about whether to codify our activities has been wide-ranging. Why write protocols that may make it easier for untrained or incompletely trained individuals to step into jobs which should be filled by genetic counselors? Who will decide the "best approach" to a complex and highly variable interaction? What force and authority will be accorded NSGC guidelines? Will written guidelines be used against genetic counselors who choose a different path, either by employers or by litigious clients? How detailed or general should guidelines be? Who will write them, review them, publish them, test them and keep them up to date? Will NSGC guidelines simply duplicate the efforts of other professional organizations? What happens in the event of conflict between guidelines?

During the course of this discussion, which took place during the turmoil of the "health care reform" era and its aftermath, it became apparent to us that our continued existence as a distinct and

economically defensible profession rested at least in part on our ability to convincingly demonstrate that genetic counselors are the most capable professionals to fill a crucial "niche" in the spectrum of health care. Though the term "physician-extender" rankles (bearing as it does an uncomfortable resemblance to Hamburger Helper™), genetic counselors can go far in defending their position on the service team by assessing the cost of similar services performed exclusively by M.D.'s, and pointing out the benefits of more thorough patient education in terms of eliciting true informed consent for testing and treatment, enhancing patient cooperation, and thus improving the likelihood of a favorable outcome. If existence equals reimbursement and reimbursement is driven by such factors as patient satisfaction, appropriate care delivery, efficient care delivery, cost savings, and (dare we say it) prevention, genetic counselors must be prepared to show how their presence on the health care team enhances these outcomes.

The lack of written guidelines for genetic counseling became painfully apparent when counselors Barbara Bernhardt and Debra Lochner Doyle were preparing supporting information for the ACMG bid for a new CPT code specifically encompassing genetic counseling. Though a number of protocols from other medical specialties referred to genetic counseling or advised genetic counseling, no authoritative protocols could be found which delineated the process or content of genetic counseling. The textbooks and articles which formed the basis of our training were available, and some clinics have devised practice manuals which set forth protocols for genetic counseling sessions, but few broadly consensual documents could be found. Also exceedingly scarce in the medical literature are outcome-based trials which assess the efficacy of the various components of genetic counseling interventions.

For help in developing a methodology for drafting practice guidelines we looked to the recommendations of the Institute of Medicine (IOM), National Academy of Sciences "Guidelines for Clinical Practice: From Development to Use", published in 1992 (National Academy Press) by the IOM Division of Health Care Services and adopted by the DHHS Agency for Health Care Policy and Research (AHCPR).

This document defines clinical practice guidelines as "**systematically developed statements to assist practitioner and patient decisions about appropriate care for specific clinical circumstances**." Guidelines are distinguished from medical review criteria, standards of quality, and performance measures, all of which have different and complementary purposes.

The IOM notes that guideline development takes place in the context of powerful economic interests; changing, sometimes conflicting notions of professional and patient autonomy; stressed, sometimes incapacitated institutions; and a continuous flow of research which simultaneously expands knowledge and uncertainty. Nevertheless, guidelines have the capacity to perform a number of important goals, including:

- assisting clinical decision making
- educating individuals and groups

- assessing and assuring quality of care
- guiding allocation of resources
- reducing risk of negligent care

Guidelines may vary in their clinical orientation, purpose, complexity, format, and intended users. The format allowing the most lucid presentation of data is preferred, and in many cases multiple modes of presentation (e.g. free text accompanied by algorithms and tables) may be successfully used. The goal is to formulate a succinct and compelling statement of professional consensus, supported by published authority, to which providers and patients may turn to make an informed choice about their options and assess their interactions in the context of contemporary understanding. By providing systematically drafted guidelines, policy makers hope to reduce the incidence of unexplained variations in care, inappropriate care, and uncertain health outcomes.

Eight attributes of good clinical practice guidelines are set forth by the IOM, including:

- **validity**(application of guideline leads to health and cost outcomes projected for it, other things being equal; guideline includes assessment of strength of evidence and projected health and cost outcomes);

- **reliability / reproducibility** ((a) given same evidence and methods, another set of experts would reach same conclusion and (b) given same clinical circumstances, the guideline is interpreted and applied in similar fashion);

- **clinical applicability** (as inclusive of appropriately defined populations as evidence permits, with explicitly stated target populations);

- **clinical flexibility** (identify specifically known or generally expected exceptions);

- **clarity** (unambiguous language, precise definition of terms, logical, easy-to-follow mode of presentation);

- **multi disciplinary process** (participation by key groups affected through panels, provision of evidence and viewpoints, review of drafts);

- **scheduled review** (recitation of temporal and / or circumstantial triggers for review);

- **documentation** (procedures, participants, evidence, assumptions, and rationales, analytic methods meticulously documented and described).

During the course of the review process, it is suggested that articles and scientific studies be placed in categories (i.e. randomized controlled trials; cohort and case-control studies; multiple time series, dramatic results in uncontrolled experiments; opinions of respected authorities based on clinical

experience, descriptive studies, reports of expert committees) and weighted according to their scientific and clinical merit. Information on reproducibility and efficacy in various clinical settings is sought. Cost / benefit analysis is performed for various options. Patient preference and patient-weighted outcome values are sought out. Attention to the process of drafting, to the real-life delivery of patient care, to the allocation of resources and to patient feedback are relatively new aspects of the historically expert-based process of guideline formulation.

The AHCPR issues competitive grants for the drafting of clinical practice guidelines with topics selected based on such criteria as potential for reducing significant variations in practice; number of individuals affected by the condition (particularly in the Medicare and Medicaid populations); adequacy of the scientific evidence to support the guideline; amenability of the condition to prevention; and cost to all payors including affected individuals. The AHCPR guideline development approach includes the following steps:

- clearly define major questions to be addressed;
- review, analyze, and rate available scientific evidence for each question;
- assess clinical benefits and harms of each intervention considered;
- review estimates of important patient outcomes for each intervention considered;
- review current and potential health costs associated with guideline, with costs when available of alternative strategies for prevention, diagnosis, treatment, management;
- invite professional, commercial and consumer comment;
- prepare draft based on available empirical evidence and on professional judgment when empirical evidence is insufficient;
- submit draft for peer review and pilot review;
- revise draft based on analysis of comments and pilot studies;
- prepare in several formats including:

    guideline report (comprehensive documentation)

    clinical practice guideline (specific statements, recommendations, algorithms, summary of evidence tables, pertinent references)

quick reference guide (summary points of prevention, diagnosis, treatment akin to protocol)

patient's guide (benefits, risks in easy to understand terms; suggested questions for health care provider)

(AHCPR Program Note, Clinical Practice Guideline Development, US DHHS Public Health Service, Rockville, MD, AHCPR Pub No 93-0023 Aug 1993)

The IOM protocol readily accommodates medical / surgical therapies and interventions; genetic diagnostic and counseling processes may not easily submit to the same type of evaluation for a number of reasons:

- Other than in the realms of prenatal and neonatal screening, patient populations are likely to be small and disparate, making systematic studies and generalizations more difficult.

- Though we expect broad consensus on a number of matters, regional practice variations are likely to arise due to demographic, cultural and geopolitical differences. Levels of care or contact easily attainable in a metropolitan setting may be impracticable in a rural area -- for example, "phone counseling" is dimly regarded by most East coasters (one commentator dubbed it an oxymoron), but it's that or nothing in many thinly settled Western states. For a subspecialty as rarified as genetics is there such a thing as a locality standard, or is our peer group national by necessity?

- Most of the clinical genetics literature is descriptive and studies comparing the relative efficacy of different counseling techniques are scarce. Outcome measures may be based on questionable assumptions (e.g. "effectiveness" of recurrence risk counseling measured by the percentage of couples electing to avoid childbearing). Expert opinion abounds but is not necessarily founded on broad experience.

- Cost / benefit assessments and important outcomes for our patients typically involve intangibles which are difficult to quantify and assign a monetary value, though we do have some idea from malpractice suits of the legally cognizable damages arising from failure to offer timely and appropriate genetic services.

- Particularly in assessing costs, benefits, and outcomes of prenatal diagnosis and other reproductive interventions we must be careful to avoid the lingering misperception that genetic services are designed to "seek and destroy" potentially costly or nonconforming lives.

- Though genetic testing is costly compared with other laboratory studies, the percentage of health care dollars currently spent for genetic evaluation, diagnosis, and counseling is unlikely to attract the attention of the AHCPR (again, with the possible exception of neonatal and prenatal screening and testing). Thus, we expect this process to be a shoestring, volunteer effort.

Tailoring the IOM recommendations to accommodate genetic counseling guidelines will demand some creativity. The NSGC lacks the resources to produce guidelines fully compliant with the IOM directives, but we believe the principles behind the directives are sound, and we intend to draft guidelines which are as faithful as possible to the letter and the spirit of the IOM directives. In addition to the immediate benefits of exploring similarities and differences in counseling practice, documenting typical practice components, and affording opportunities for improving skills, we believe that drafting and promulgating practice guidelines will sharpen future research efforts, providing a starting point for the systematic evaluation of genetic counseling practices.

In developing guidelines for specific clinical situations we intend to emphasize those elements of genetic evaluation and care which are particularly in the realm of genetic counselors. These may include special considerations in eliciting a family pedigree and medical history; collaborating with the genetics team in explaining and arranging recommended diagnostic studies; presenting medical information and client options specific to a diagnosis; engaging in psychosocial counseling; linking families to support mechanisms, and the like. Genetic services which are currently managed primarily by genetic counselors (e.g., prenatal counseling) are logical starting points.

The American College of Medical Genetics is engaged in drafting practice guidelines which are expected to emphasize diagnostic processes and medical interventions, though by no means ignoring counseling issues. Genetic Counselor associate members of the ACMG serve on the Clinical Practices committee and an NSGC liaison to the College is in place. Members of the ACMG Clinical Practices committee will review and comment on NSGC guideline drafts. We expect these documents to dovetail nicely.

Our guideline development protocol, which is still a "work in progress", will likely proceed along the following lines:

1. **Identification of topic**

Early choices are expected to include commonly encountered clinical situations with generally broad consensus of approach and a relatively rich supporting base in the literature. Emphasis will be given to clinical conditions for which genetic counselors perform the bulk of services. Disease-specific guidelines are anticipated which may include medical and phenotypic features sought during pedigree construction; discussion of various diagnostic and treatment options and familial issues attendant thereto; review of patient education materials and support groups. As new avenues open for genetic counseling services (such as cancer counseling), guidelines will emerge as important teaching tools.

2. **Identification of authors**
Ideally at least three authors from at least two different institutions will participate in the literature review and drafting process. This rather small cohort allows for distribution of the burden of research without diffusion of responsibility; expands opinion and judgment; enhances the likelihood that a broad range of counselor practices will be considered; and minimizes cumbersome and costly logistical difficulties. We are likely to rely on "emergent leaders" who respond to general invitations to draft guidelines in areas of expertise. We are also likely to seek authors on the basis of peer recognition and representation in the scientific literature. Finally, the newly established Special Interest Groups within the NSGC may prove to be a rich source for guideline drafting.

3. **Identification of peer reviewers**
At least three genetic counselors not involved in the drafting process will be asked to review draft guidelines. Peer reviewers ideally will represent diverse institutions and geographic areas and will be identified in the early stages of drafting. Peer recognition of expertise, suggestions of the drafters and suggestions of outside authorities will be considered in inviting peer reviewers.

4. **Identification of consumer participants/reviewers**
When pertinent patient support groups exist, these groups should be invited early in the process to comment on content and to review draft guidelines. Individuals and families known to the drafters or reviewers may also be invited to comment and review.

5. **Identification of specialist participants/reviewers**
Representatives of the ACMG Clinical Practice Committee will review each draft guideline. In many cases the opinion and review of other specialists will be sought during the course of drafting -- e.g. pulmonologists, perinatologists, opthalmologists, oncologists, clinical and molecular geneticists, etc. Specialists are likely to be known to the authors and may have a working relationship with them. When possible the opinion of at least one specialist from an independent clinical group will be solicited.

6. **Literature search and review**
The authors will conduct a literature review and assess the nature and merits of pertinent publications. Personal communication with recognized authorities may also be sought and cited, particularly when publications are scanty. Guidelines from other professional groups will be evaluated. Information regarding incidence, diagnostic options, treatment options, prevention options, cost considerations, quality of life issues, psychosocial issues, legal and ethical issues, educational resources and support resources will be sought as appropriate. Comments of the previously identified interest groups will be considered.

7. **Drafting of guideline**
The guideline may be in any format suitable for lucid presentation of the data. We expect many will take the form of free text with supporting algorithms and tables. We do not anticipate issuing separate guidelines for professionals and lay people though authors may choose to develop patient information

documents in concert with the practice guideline if it is determined that existing patient information is deficient. A prototypic guideline might include the following elements:

- purpose of guideline
- objectives of guideline
- brief recitation of methodology, type and strength of evidence
- synopsis of the clinical condition
- primary counseling considerations
- pedigree drafting
- likely diagnostic options
- when appropriate?
- risks and benefits of each
- cost considerations
- psychosocial ramifications
- counseling issues associated with diagnosis
- diagnostic certainty
- phenotype / genotype
- natural history
- medical and developmental concerns
- treatment options
- degree of consensus among experts, literature
- empirical support for each option
- risks and benefits of each option
- cost issues to society and family
- psychosocial ramifications
- recurrence chances
- reproductive options
- opportunities for prevention
- family-oriented literature
- family-oriented support groups
- social service considerations
- documentation / patient summary letter
- communication with referral source
- summary and recommendations
- triggers for review of guideline
- boilerplate disclaimer
- citation of references

Authors may also choose to include a practice protocol briefly outlining the typical course of a counseling session to serve as a checklist or quality tool as appropriate. This process is expected to take 4 to 6 months.

8. **Review of draft by peer counselors, Genetic Services Committee chair, Clinical Practices Subcommittee chair, Ethics committee**
Before outside review is conducted, these individuals will determine whether the draft meets the general criteria for guideline scope and content, presents information in an understandable fashion, and in the opinion of the peer reviewers soundly reflects current counseling practice. If significant concerns are raised, comments are received and integrated by the authors whereupon a second peer review occurs. This process is expected to take 1 - 2 months.

9. **Review of draft by ACMG, specialists, consumers, legal counsel**
Following approval by peer reviewers the final draft is submitted to outside reviewers for formal comment. If significant concerns are raised, comments are received and integrated by the authors whereupon a second peer review occurs followed by a second outside review. This process is expected to take 1 - 2 months.

10. **Publication**
Several publication possibilities exist, including the Journal of Genetic Counseling, the Perspectives newsletter, or a looseleaf service. We currently envision distributing the guidelines as punched inserts to the Perspectives newsletter, which counselors can retain in a notebook form and easily keep up to date. Non-members or new members would be able to order copies through the NSGC publications division.

The final hurdle, field testing, probably will be beyond the scope of the NSGC but we are hopeful that the publication of the guidelines will inspire clinical evaluation and feedback. We also expect commentary from the general membership of NSGC which, following a recent lively exchange regarding the wording of a position statement, is probably inclined to read NSGC publications very carefully.

CORN and the state departments of health can be of assistance in the process of practice guideline development in a number of ways. The traditional roles of gathering and disseminating information about needs, priorities, required resources, costs, and impediments to delivery of service are critical to the formulation of useable guidelines. CORN may also be a logical meeting ground for the various professional groups, to assure the right hand knows what the left hand is doing. Once a guideline has been promulgated, CORN may be in a position to assist in establishing field testing and clinical trials to judge efficacy. Finally, when a guideline has proved its mettle, CORN might champion its use in quality assurance and assist in the public and professional education process.

Certification, Credentialing, and Licensure
Other potential avenues to ensure proficiency among genetic counselors are the processes of certification, credentialing, and licensure. As noted above, the board certification of master's level genetic counselors is managed at the national level by the American Board of Genetic Counselors. This body determines the eligibility of applicants to take the boards as well as setting standards and determining compliance of training programs.

National board certification currently carries no legal significance in most states, the notable exception being California in which prenatal testing centers are required to have access to a board certified or board eligible genetic counselor. For many years certification also carried little significance with regard to hiring and compensation, with the result that a sizeable percentage of practicing genetic counselors have never sought certification.

Despite this lack of oversight as to the qualifications of genetic counselors, it is probably safe to say the majority of complex genetic counseling in this country is delivered by specialist M.D., Ph.D. or Master's level personnel. In specialty clinics, single-gene counselors and educators may lack even a bachelor's degree, but most have sharply limited scopes of practice as well as reasonably close supervision.

The spectacular rise of cancer genetics testing and counseling by non-geneticists has shown that non-specialist entry into the genetic counseling realm will not be confined to those disorders which are straightforward, readily understood and readily explained. From the standpoint of public protection, the need for some type of oversight on those offering genetic testing and counseling now seems more compelling.

For those professions in which lengthy and competitive academic training is required, the trend appears to be towards national board certification. State licensure is then issued on the strength of the national boards and periodic renewal may be dependent on demonstration of CEU's. For many other regulated service providers, particularly those disciplines which do not involve extensive academic preparation, passage of state-administered qualifying exams is still the norm.

Periodically, interest in state licensure has arisen among genetic counselors when a state has undertaken to regulate the use of the term "counselor" and/or the provision of "counseling services," be they psychotherapeutic, financial or otherwise. Though genetic counselors have to date fallen outside the scope of these licensing provisions, many have been worried, at least transiently, that their practices may run afoul of the law. In several states genetic counselors have made inquiries about separate licensure and have been rebuffed by the predictable responses: there is no demonstrated public health risk; the number of practitioners is too small to warrant a licensing program; genetic counselors practice only under the supervision of physicians and therefore do not require separate licensure; counselors are merely attempting to limit competition.

As public interest in genetics burgeons and demand for testing soars, the resources of traditional service providers are likely to be outstripped. Other medical specialties will incorporate genetic services into their practices. Direct marketing to the public of certain types of commercially available genetic services has already occurred and can be expected to continue. Help will be needed in documenting the provision of genetic services by nontraditional providers, and in following the outcome of such interactions to determine whether adequate service has been delivered.

If it can be demonstrated that misinformation, misdiagnosis, delayed or inadequate care, or other adverse outcomes disproportionately result in the hands of non-geneticists, serious consideration should be given to mandatory training, certification or licensure of individuals offering genetic services and genetic counseling.

Knotty issues surrounding this process will include, but not be limited to, the possibility of requiring special training, certification, registration or licensure for non-geneticist physicians, nurses, allied health professionals and health educators who offer certain genetic services; the possible need for stratified training, certification, registration or licensure so that non-geneticists could attain credentials in particular sub-specialties; the chance that as the field becomes more complex, board-certified geneticists and genetic counselors should likewise be compelled to satisfy certain training requirements before performing certain types of services; the establishment of continuing education requirements for licensed, registered or certified practitioners; the matter of grandfathering or otherwise extending "credit" to current practitioners who are not boarded; and the potential adverse impact on public access to genetic services as a result of such measures.

The documentation of health care needs, service provision patterns and outcomes falls squarely within the mandate of the public health service. The NSGC would eagerly participate in a systematic analysis of licensure issues for genetic counselors. The NSGC would also encourage CORN and the state departments of health to collaborate in projecting client needs and desires for genetic services, predicting workforce requirements, determining appropriate client loads for various genetics professionals, and developing innovative methods of providing services in challenging settings.

Many elements contribute to the process of assuring that people receive the right services at the right time, delivered by the right person at the right cost. The National Society of Genetic Counselors has made a commitment to expend a considerable proportion of its volunteer resources to help attain these goals in the realm of genetic counseling. We welcome invitations to collaborate in this endeavor.

Health Supervision for Children with Heritable and Congenital Disorders

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Introduction

The mission of the American Academy of Pediatrics (AAP) is the attainment of optimal physical, mental and social health for all infants, children, adolescents, and young adults. Its membership comprises approximately 50,000 physicians including pediatric medical and pediatric surgical subspecialists and pediatric residents in training. About 30,000 or 60% of the membership are actively engaged in the primary care practice of pediatrics in the United States. Currently, there are approximately 300 board certified pediatricians who are also certified by the American Board of Medical Genetics; most of whom are members of the Academy's Section on Genetics and Birth Defects. The Committee on Genetics of AAP is composed of 6 members representing 6 of the 9 Academy's regional districts with liaison representation from the National Institute of Child Health and Human Development, Federal Health Resources and Services Administration -Department of Health and Human Services, Centers for Disease Control and Prevention, American College of Medical Genetics, American College of Obstetrics and Gynecology, and the Academy's Section on Genetics and Birth Defects.

The directives to the Committee on Genetics include the preparation for publication in the Committee's area of expertise information for the generalist pediatrician in areas not readily or concisely available elsewhere and which will be useful to a majority of the membership of the Academy.

Although genetic disorders individually are relatively uncommon; in the aggregate they account for significant morbidity and mortality during infancy and childhood. The following statistics are often cited:

- ✓ 1:170 live births with a chromosomal abnormality
- ✓ 2-3% of live births with a major congenital malformation
- ✓ congenital malformations are the leading cause of death under 1 year of age; second under age 5 years
- ✓ accounts for 1/3 of hospitalized children in tertiary care centers
- ✓ 3% of school aged children are cognitively disadvantaged

Health Supervision for Infants and Children

The Academy of Pediatrics had developed a framework of health maintenance for infants and children entitled, *Recommendations for Preventive Pediatric Health* --- essentially a periodicity schedule for pediatricians. Simply put, it outlines how frequently health supervision visits should occur, concentrates on the specific interval history and physical examination content required to monitor the child's general health, growth and development (eg, hearing and visual screening, developmental milestones, dental examinations, blood pressure measurement) and suggests appropriate age-related anticipatory guidance (eg, discussion of infant feedings, immunizations, accident prevention strategies, normal developmental progress, school readiness, etc) (Table I).

Despite the aforementioned relative rarity of individual genetic disorders and birth defects, many pediatricians and family practitioners will certainly be called upon to be the primary care physician for children with Down syndrome and almost certainly will have children with some of the more common genetic disorders in their practice. With the current emphasis on the primary care provider as being the gateway to specialty care, more of the "routine care" will be provided by the generalist with the specialist used more as a resource problem solver, manager of specific co-morbidities, and educator regarding cutting-edge diagnostic and treatment strategies. All children with disabilities require routine health care, immunizations, and knowledgeable discussion with parents concerning the nature of the disorder, short and long range complications and morbidities, emergence of other health related issues, and transition into adulthood; in short, the usual anticipatory guidelines for any child with an added emphasis on problems specific to that congenital disorder. With this in mind, the Committee on Genetics has developed a series of Health Supervision for common congenital disorders utilizing the same time frames as the Academy's routine health maintenance visits with the appropriate additional health supervision and anticipatory guidance for the specific disorder.

Thus, for this series of congenital disorders, there is an overall discussion of the condition followed by focused recommendations at various health maintenance visits:

- Prenatal or preconceptual visit (if the parents are aware that they are at risk for a heritable disorder).
- Neonatal visit (or initial visit when the diagnosis has been established).
- Infancy: 1 month to 1 year (5 visits)
- Early childhood: 1-5 years (5 visits)
- Late childhood: 5-13 years (annual)
- Adolescence: 13-21 years (annual)

Since 1992, the following disorders have been formatted in this way (Table II).

Each statement begins with a description of the phenotype (Table III - Down syndrome; Table V - Turner syndrome) and follows with specific health supervision focused at various time intervals. Thus, health supervision for children with Down syndrome and Turner syndrome, for example, can be incorporated into the health maintenance schedule as shown in Table I and depicted in Table IV (Down syndrome) and Table VI (Turner syndrome).

Additionally, areas of ongoing assessment throughout childhood require periodic review at developmentally appropriate ages. These include the following and are generic to all the statements:

- Review personal support available to family.
- Periodically review other financial and medical support programs for which the child may be eligible.
- Discuss filing for Supplemental Security Income (SSI) benefits.
- Discuss injury prevention with special consideration of developmental skills.
- Discuss diet and exercise to maintain appropriate weight.

Following the completion of these statements and the Newborn Screening Fact Sheet, it has been proposed to publish this series in a supplement to *Pediatrics* --- possibly in a binder format which can be used as a reference guide for the physician and individual disorders copied and placed in the patient's folder for easy reference.

Discussion

Physician Concerns

A number of concerns have been raised regarding the potential utility of such health supervision statements. They have involved the following areas and have been raised by both primary care pediatricians and specialty pediatricians. All statements contain the following:

- Policy statements do not indicate an exclusive course of treatment but are meant to supplement anticipatory guidelines available for treating the healthy child provided in the AAP publication "Guidelines for Health Supervision".
- The statements are intended to assist the pediatrician in helping children with genetic conditions to participate fully in life.
- Diagnosis and treatment of genetic disorders are changing rapidly; therefore, pediatricians are encouraged to view these guidelines in light of evolving scientific information.

- Clinical geneticists may be a valuable resource for the pediatrician seeking additional information or consultation.

Nonetheless, the following unresolved issues remain which may be generic in any attempt to publish health supervision recommendations or guidelines. Several are addressed below.

Medico-legal aspects
A test is recommended in the guidelines and not performed, not performed during the time suggested or not repeated at the prescribed intervals.

What is the standard to which a pediatrician may be held as opposed to the family physician or "general standard of care"?

Resolution of differences of opinion
Obviously, there will be some ambiguities and differences of opinion among specialists. Some of the issues raised to the Committee have included frequency of echocardiogram study in children and adolescents with Turner syndrome; does the infrequency of morbidity with minor cardiac valve involvement justify the cost of the repeat echocardiogram; how does one get an adequate ECHO in an infant without the need for sedation which could pose an added risk; what is the appropriate hearing screen test for an infant?

Obviously, these important issues need to be addressed and broad review of these statements by appropriate specialists have been part of their development. Statements developed in 1992 are only now being published. They will undoubtedly require updating and modification. It is anticipated that a binder format will allow for additions, updates and modification of these statements.

In conclusion, I should like to comment on the role of the genetic specialist as he or she relates to the primary care physician in the management or co-management of relatively uncommon disorders. The body of genetic knowledge is unique, evolving rapidly, pervades both primary and subspecialty care and is required for the comprehensive management of infants and children with special needs. Genetic specialists enhance pediatric training programs, provide education, awareness and relevance of genetics for practicing pediatricians, and serve as a valuable resource in the management of the special health care needs of children. These health supervision statements highlight the educational and interactive role of the clinical geneticist in clinical practice.

Table 1

Table 2

Health Supervision
A. Published in *Pediatrics*: ■ Down syndrome 93:855, 1994 ■ Achondroplasia 95:443, 1995 ■ Neurofibromatosis 96:368, 1995 ■ Turner syndrome 96:1166, 1995
B. In review: ■ Marfan syndrome ■ Fragile X ■ Sickle cell disease
C. Of related interest: ■ Newborn screening for hypothyroidism 91:1203, 1993 ■ Newborn screening fact sheet (in review)

Table 3

Down syndrome phenotype: Associated significant abnormalities	
Mental retardation	IQ 50-70 usual
Congenital heart disease	50%
Serous otitis media	50-70%
Deafness	75%
Gastrointestinal atresias	12%
Severe refractory errors	50%
Cataracts	15%
Thyroid disease	15%
Acquired hip dislocation	6%
Hirschsprung's disease	1%
Leukemia	1%

Table 4

HEALTH SUPERVISION FOR CHILDREN WITH DOWN SYNDROME - COMMITTEE ON GENETICS*

	Infancy, 1 mo - 1 yr						Early Childhood, 1 -5 yr							
	Prenatal	Neonatal	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	4 y	Late Child-hood,5-13y, Annual	Adolescence, 13-21 y, Annual
Diagnosis														
Karyotype review ǂ	▌	▌												
Phenotype review	▌	▌												
Recurrence risks	▌	▌												
Anticipatory guidance														
Early intervention services	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌			
Reproduction options	▌↕	▌↕	▌↕				▌				▌			
Family support	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌
Support groups	▌	▌	▌				▌							
Long-term planning	▌						▌						▌§	▌§
Sexuality													▌	▌
Medical evaluation														
Growth		0	0	0	0	0	0	0	0	0	0	0		
Thyroid screening		0¶			0		0			0	0	0		
Hearing screening			S/0	S/0	S/0	S/0	S/0↕			S/0↕	S/0↕	S/0↕	S/ §	S/
Vision screening		S/0	S/0	S/0	S/0	S/0↕	S/0			S/0	S/0	S/0	S/ ‖	S/
Cervical spine roentgenogram											0**			
Echocardiogram	▌	0												
Psychosocial														
Developmental & behavioral	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/	S/
School performance										0	0	0		
Socialization							S						S	S

*Assure compliance with the American Academy of Pediatrics "Recommendations for Preventive Pediatric Health Care".
▌ = to be performed; S = subjective, by history; and 0 = objective, by a standard testing method
ǂ Discuss referral to specialist
§ Give once in this age group
¶ According to state law
‖ As needed
** See discussion

Table 5
Clinical Abnormalities in Turner Syndrome*

	Approximate Incidence (%)**
Short stature	100
Gonadal dysgenesis with hypoplasia or aplasia of germ cells	>90
Edema of hands and feed	>80
Broad chest with inverted or hypoplastic nipples	>80
Unusual shape and rotation of ears	>80
Narrow maxilla including palate	>80
Micrognathia	>70
Inner canthal folds	>40
Low posterior hairline with appearance of short neck	>80
Webbed neck	50
Cubitus valgus or other elbow anomaly	>70
Knee anomaly (e.g., tibial exostosis)	>60
Short metacarpals or metatarsals (usually 4th)	>50
Pigmented nevi	>50
Cardiac anomalies	>20
Mostly bicuspid aortic valve, coarctation of aorta, aortic valve stenosis, also hypoplastic left heart, mitral valve prolapse dissecting aortic aneurysm (rare)	
Renal anomalies	>60
Mostly horseshoe kidney, duplicated renal pelvis, ectopic or malrotated kidney, or vascular anomalies	
Central nervous system	>50
Hearing loss	
Occasional abnormalities	
Dysplastic hip	
Madelung deformity (radial deviation of hand because of abnormal ulnar or radial growth)	
Scoliosis	
Kyphosis	
Vertebral fusion	
Ptosis	
Strabismus	
Blue sclerae	
Cataract	
Hemangiomata (rarely of intestine)	
Tendency to form keloids	
Tendency to obesity	
Idiopathic hypertension	
Diabetes mellitus***	
Abnormal glucose tolerance	
Crohn disease	
Thyroid disorders	
Ulcerative colitis	

* Modified from Jones KL., ** Incidence figures in published studies vary with source of data and population characteristics.
***Controversial. See text.

Table 6

HEALTH SUPERVISION FOR CHILDREN WITH DOWN SYNDROME - COMMITTEE ON GENETICS*

	Infancy, 1 mo - 1 yr							Early Childhood, 1 -5 yr						
	Prenatal	Neonatal	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y	4 y	Late Child-hood,5-13y, Annual	Adolescence, 13-21 y, Annual
Diagnosis														
Karyotype review ǂ	▌	▌												
Phenotype review	▌	▌												
Recurrence risks	▌	▌												
Anticipatory guidance														
Early intervention services	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌			
Reproduction options	▌↕	▌↕	▌↕				▌				▌			
Family support	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌	▌
Support groups	▌	▌	▌				▌							
Long-term planning	▌						▌						▌§	▌§
Sexuality													▌	▌
Medical evaluation														
Growth		0	0	0	0	0	0	0	0	0	0	0		
Thyroid screening		0¶			0		0			0	0	0		
Hearing screening			S/0	S/0	S/0	S/0	S/0↕			S/0↕	S/0↕	S/0↕	S/ §	S/
Vision screening		S/0	S/0	S/0	S/0	S/0↕	S/0			S/0	S/0	S/0	S/ ‖	S/
Cervical spine roentgenogram											0**			
Echocardiogram	▌	0												
Psychosocial														
Developmental & behavioral	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/0	S/	S/
School performance										0	0	0		
Socialization							S						S	S

*Assure compliance with the American Academy of Pediatrics “Recommendations for Preventive Pediatric Health Care”.
▌ = to be performed; S = subjective, by history; and 0 = objective, by a standard testing method
ǂ Discuss referral to specialist
§ Give once in this age group
¶ According to state law
‖ As needed
** See discussion

Ackowledgments

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A Project to Develop, Disseminate, and Evaluate Two Clinical Guidelines in Medical Genetics for NYS

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The New York State Department of Health has awarded a grant to the American College of Medical Genetics Foundation for a project entitled: "Development, Dissemination and Evaluation of Two Clinical Guidelines in Medical Genetics". These funds will enable the College to bring together working groups of genetic service providers, representatives of medical specialty societies, "consumers" of genetic services, and others to develop, distribute, and evaluate two clinical guidelines: one on appropriate breast/ovarian cancer genetic counseling, screening, testing and follow-up, and the second on evaluation of the newborn with single or multiple congenital anomalies. In general, projects supported under this NYS initiative aim to (1) develop guidelines in areas of potential over or underuse, or in areas having significant potential for quality problems; (2) identify and test effective models for guideline dissemination and implementation; and (3) translate technology assessment findings into guidelines.

The grant project is based in the Genetic Services Program, Wadsworth Center, New York State Department of Health. The guidelines will target New York State provider populations, but may serve as a model for interested parties in other states. Project oversight will be provided by the Joint Committee on Professional Practice and Guidelines of the College, whose chair is the project's Principal Investigator. Consultants knowledgeable in clinical guideline preparation and utilization will lend their expertise to the process. The project is expected to be completed in a two-year time period.

A project coordinator has been hired and initial planning has begun. A letter has been sent to the presidents of various professional societies and other organizations considered to be stakeholders in these two areas, including the:

- American Society of Human Genetics
- National Society of Genetic Counselors
- International Society of Nurses in Genetics
- American Academy of Pediatrics
- American College of Obstetricians and Gynecologists
- American Public Health Association
- Alliance of Genetic Support Groups
- National Association of Breast Cancer Organizations
- American College of Surgeons
- American Society of Clinical Oncologists
- Organization of Teratogen Information Services
- Council of Regional Networks for Genetic Services.

Representatives of these groups will make up the Steering Committee, which will make final decisions about the makeup of the six working groups providing development, dissemination and evaluation functions.

Other activities include: (1) assembling a library of journal articles and other materials in the two substantive areas and in the area of clinical guideline development; (2) conducting a wide-net search for potential consultants from private consulting firms, academic, and government-based institutions; (3) presenting at the December meeting on "Cancer Genetic Services in the GENES Region"; and (4) submitting an abstract for the 1996 American Public Health Association Annual Conference, to be held in November in NYC.

Financing Genetics Services: Mendel's Paradox

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One of the drawbacks in giving a talk about financing any type of medical service in a time of health systems chaos and transition is the risk of sounding negative and pessimistic. Therefore, I want to reassure you at the onset that I will be presenting initiatives which I believe signal areas of growth and optimism for medical genetics.

The infrastructure for financing medical genetics services is carried out on both national and local platforms. You may remember this model system we created for two separate Maternal and Child Health Bureau (MCHB) funded projects on reimbursement for genetics services (1984 and 1987). The "ecosystem" model identifies both macro, as well as micro system components of the health care delivery system. The macro system contains federal and state legislative initiatives, agencies, and programs, while the micro system represents the actual medical genetics delivery system at the local, regional, and national levels. Central to the ecosystem model, however, is the relationship between patients, employers, and the health insurance system. The rapid emergence of the managed care system has significantly altered the relationship of patients to employers, patients to providers, and employers to health insurance companies. In fact, there is now a significant number of employers who are also self-insuring for their own employees. These self-insuring companies currently exist largely outside of state and federal insurance regulations.

The national sources of financing genetic services represent various federal legislative programs, as well as health care financing structures (Table 1). As you can see from this list, there are examples for federal programs, such as Medicare, Medicaid, Title V funding for MCHB, federal funding of the National Institutes of Health, which also includes The Human Genome Project initiative and its various subsections. In addition, there are federal agencies, such as the Health Care Financing Administration (HCFA), which administrate Medicare, Medicaid, and the resource-based relative values scale (RBRVS) which dictates the manner in which reimbursement will flow for various types of medical services. Finally, the American Medical Association's (AMA) Current Procedural Terminology system, the CPT codes, are an example of a national coding system for identifying those services provided by physicians.

One important aspect of federal funding, the Medicaid program, is an issue that is of great concern to all of us here today (Fig. 2). The Council of Regional Genetics Networks (CORN) is dedicated to improving the utilization and accessibility of medical genetics services for those members of our society who represent the eligible population, that is, our public health genetics program. As you can see, the cost of the Medicaid program continues to increase annually so that the current debate is now focused on how much of this cost will now be down-loaded in the form of block grants to the states. This will have special significance to us for the continued availability of medical genetics services as part of the Medicaid managed care system.

However, my particular focus today is more on financing medical genetics services at the local provider level (Table 2). The local provider of medical genetics services at the medical school, community hospital, or state health department is dependent upon income generated from clinical service, laboratory service, extramural research grants, state health department grants and/or contracts, as well as institutional support. You are all well aware of the changing proportions among these categories, particularly the increase in clinical service responsibility. These proportions are reflective of national, regional, and local health care system changes.

With regard to the issue of clinical service delivery, medical geneticists are being asked by their employers to generate an increasing proportion of their salaries from clinical services. Reimbursement for professional services is dependent upon a number of different factors. The financial value of the service is dependent upon a national volume assessment by HCFA, which is then related to the establishment of local fee schedules and communicated through the CPT and ICD-9 diagnostic coding systems. The validity of the reimbursement system is now, more than ever, dependent on appropriate documentation of utilization, medical necessity, and efficacy.

Through our previous MCH SPRANS grants on reimbursement, of the individual CORN regions, and, more recently, the American College of Medical Genetics have each attempted to educate medical genetics providers and their administrators on how to appropriately code for reimbursement of medical genetics services.

We have stressed the necessity of identifying medical genetics services as a consultation service based on the AMA recognition of medical genetics as a bona fide medical specialty. The CPT manual describes the key components of this consultation service (Fig. 3).

Fee schedules are, therefore, constructed on the basis of the comprehensiveness and complexity of the consultation. While time is not identified as a key component, it is clear that the medical geneticist uniquely spends a considerable amount of time during a typical genetics consultation. The cost effectiveness of the medical geneticist and the services that care provides in the health care system have yet to be accurately determined.

If you are comfortable with analogies, consider this one from a baseball perspective. The American Board of Medical Specialties of the AMA has invited us into the "game" as a player. The American College of Medical Genetics has given us the uniform. The CPT codes give us the bat to swing. The managed care system, the "manager", may or may not give us a chance to come up to bat or play at some designated position, in spite of our talent and ability.

Laboratory service income has long been the backbone or "cash cow" for many medical genetics units (Fig. 4). However, significant changes in the transition of high technology laboratory services from the academic center to the commercial sector continues to significantly disrupt this income source. Since 1986 there has been a significant increase in the role of commercial laboratories in providing highly competitive, comprehensive laboratory contracts to the managed care system (Fig. 5). Academic genetics

laboratories, and even specialty genetics companies, continue to lose substantial proportions of their market to the ever-increasing size and competitiveness of the mega labs. Therefore, the academic service laboratory has less income to share with its clinical service and its role as a site for fellowship education is also seriously threatened. Many of us have recent anecdotal experiences with the loss of test and report quality, increased turn-around time for amniocentesis reporting, and the absence of medical genetics interpretation and professional consultation from these labs.

With regard to other sources of income, such as research and training grants, we are all aware of the shrinking pool of research and development dollars available to support investigators' salaries, as well as to fund the next generation of teachers through fellowship support. The American Society of Human Genetics has identified for the first time this year a section on the dues-membership application to indicate where investigators now obtain research support (Table 3). Future years will enable us to follow this changing profile, but certainly the fact that less than half of the respondents filled out this section would suggest that they had little to report.

Before leaving this section and moving on to operational initiatives that would address ways to improve the financial status of medical genetics units, we need to further explore the changing health care system as it affects the delivery of medical genetics services. To remind you, the various players in this system include the patients, the providers, the health insurance companies, as well as the employers who buy their policies, and the federal and state agencies who create the legislative infrastructure (Fig. 1). Within this system, therefore, we can quickly remind ourselves of who is, in fact, paying for the medical care system. We see once again that there are over 40 million people who have no health insurance, that only 29% of current policies cover dependents, and that Medicaid continues as a major funding source for the population of disabled and elderly (Fig. 6).

The delivery system is clear in conveying to us the fact that managed care/HMO's are being employed rapidly to an increasing degree across all types of payers (Fig 7). We also know that the total number of HMO's are declining as various HMO companies become larger and larger national providers. Although the number of physicians signing-up to participate in managed care networks has moved forward at different rates in different regions of the country, in the last three years the rate of change has become more significant. Since 1992 the number of physicians who are joining some type of health care network has grown from 56 to 90% (Fig. 8). This tells us that the predominant health care mode of delivery will be managed care networks, driven principally by primary care gate keepers.

It is also of importance to understand that capitation through managed care networks is growing in influence and will dictate how many specialists will be able to practice in a given geographic area (Fig. 9). Primary care providers will contribute substantially to decisions about how many medical geneticists will be able to practice in a given region. Capitation is already a significant component of Medicaid managed care and will become even more so for Medicare, as well.

One other area of development that we should become more aware of is the influence of managed care on the pharmacy, i.e., the relationship of the physician to the patient through his/her ability to prescribe

medications (Fig. 10). For the medical geneticist, this has become an increasing problem once again for those of us who must prescribe metabolic products for individuals identified in the newborn screening programs. The resistance of the subcontracted pharmacy by the managed care system to honor and/or respect the need to treat individuals with inborn errors of metabolism is now seriously threatened.

But it is time to move away from the apparent quicksand of a health care system that is becoming less user friendly for specialists, such as the medical geneticist. Let us examine four areas in which current initiatives show signs of healthy optimism: (1) initiatives by state health departments, particularly in the area of Medicaid; (2) the use of clinical guidelines to secure the place of medical genetics at the reimbursement table; (3) systems reengineering or reorganization to permit medical geneticists to exercise more control over the reimbursement process; and (4) the development of reference laboratory alliances to secure consistent laboratory income.

Various health departments have taken initiatives to begin to solve some of these problems. I will only mention four, but it is obvious that many states are moving forward at different rates in imaginative and effective ways (Table 4). TexGene, working with Texas Medicaid, developed an entire set of their now famous "G codes" that enabled them to secure appropriate rates of reimbursement for professional, procedure, and laboratory services. More importantly, Mary Jo Harrod has shown how to broker trade-offs between Title XX, Family Planning, and Title V programs with regard to the rate of federal reimbursement. In California, George Cunningham is now legendary in his efforts to provide high quality, accessible prenatal genetics services through state statute and regulation. Cindy Curry has provided additional clarity in developing clinical guidelines for the delivery of medical genetics services. In Washington state, Bob Fineman and Deb Doyle, working out of the health department, have developed a registration system for genetic counselors enabling them to attain state provider status and, thus, improve the availability and accessibility of medical genetics services throughout the state.

More recently, Carolyn Bey and Suzanne Cassidy, working with Ohio Medicaid, have applied the Texas model to their successful development and implementation of improved reimbursement for medical genetics services in their state. They have defined special genetics services in the Medicaid provider handbook (Tables 5 & 6). They have also developed additional codes that improve the rate of reimbursement. In particular, stacking codes for pedigree construction, psychosocial genetic assessment, and medical genetic counseling will now permit an increased rate of reimbursement for the Medicaid population. Many of us have found it difficult to continue to provide services when the rate of reimbursement for Medicaid has been so low. Their example should encourage us to keep trying.

The second mechanism that medical geneticists need to pursue is the development of clear, defensible, and cost effective clinical guidelines for the services delivered. Clinical practice guidelines are being developed rapidly by many medical disciplines, particularly those with full time paid administrative staffs. At last count, the American College of Medical Genetics listed only 850 M.D. geneticists and the American Board of Genetic Counselors listed 850 genetic counselors compared to 10,000 pathologists. The College has recently been awarded a grant to develop guidelines for the delivery of services in breast cancer genetics and for the child born with a birth defect. It is clear that the managed care system is

seeking such clinical guidelines in order to establish rules for payment on medical necessity and clinical efficacy (Fig.11). It is incumbent on our specialty to pursue this particular avenue more aggressively and consistently.

The third initiative to consider is the reengineering or reorganization of management models for the delivery of medical services. The integration of primary care and specialist physicians into various delivery models now occupies a good deal of our time and attention. In fact, whether or not we will be employed by a particular regional network is an issue that we have never had to contend with in the past. The role of the specialist, such as the medical geneticist, as a hospital-based versus an ambulatory-based specialist needs to be evaluated carefully (Fig. 12). The growing influence of primary care networks tells us that the number of dollars to be allocated to hospital-based specialists is declining. Medical genetics is largely an outpatient specialty. Therefore, we should give serious consideration to restructuring our location to outpatient or ambulatory structures and not continue to carry on our shoulders the significant costs of hospital overhead and its indirect costs. Regional or national alliances of medical geneticists have been suggested as one approach to this issue.

Finally, I alluded previously in this talk to the vulnerability of the academic genetics service laboratory to the growing mega commercial environment as one of the most serious threats to the integrity of the delivery of medical genetics services as they are now constructed. One recent suggestion has been to establish a regional core of collaborative laboratory services from among the region's hospitals (Fig. 13). This would permit regional hospitals to create local shared, comprehensive services that would be cost effective and competitive with the national mega labs. Laboratory genetics services would be included in this structure and, therefore, receive program protection. A local HMO who buys services from the local comprehensive medical service provider (PHO, MSO, PCP, etc.) will now also receive comprehensive services from the laboratory alliance that includes the local genetics laboratory. This could stabilize laboratory income for the genetics unit and preserve their local responsiveness to patients and physicians.

Financing health care delivery in the United States will continue to be a challenge for some time to come. Financing medical genetics services within this system will be equally challenging. It will take our imagination, energy, and collaboration to be successful. More importantly, it will require our collective commitment, particularly if the public health sector exemplified by the CORN experience leads the way.

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Figure 1

Table 1

FINANCING GENETIC SERVICES
National System • Medicare • Medicaid • Title V (MCHB) • Title XII (Family Planning) • NIH • Human Genome Project • HCFA (RBRVS) • AMA (CPT coding)

Figure 2

Table 2

FINANCING GENETIC SERVICES
Local Provider • Clinical income • Laboratory income • Extramural grants (research/development) • State Health Department grants/contracts • Institutional support (medical school/hospital)

Figure 3

99245 Office consultation for a new or established patient, which requires these three key components:

a comprehensive history;

a comprehensive examination;

and medical decision making of high complexity.

Counseling and/or coordination of care with other providers or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs.

Usually, the presenting problem(s) are of moderate to high severity.
Physicians typically spend 80 minutes face-to-face with the patient and/or family.

Figure 4

Figure 5

Table 3

ASHG DUES MEMBERSHIP QUESTIONNAIRE

Sources of Research Funding, 1995-96

	Number
NIH	640
Private foundations	494
Institutional	364
State	353
Other national agencies	276
Private industry	157
Postdoc fellowships	112
NIH training grant	108
Province (Canada)	64
NSF	29

Table 4

LEARN FROM SUCCESSFUL INITIATIVES

1. Texas Medicaid	Mary Jo Harrod
2. Ohio Statewide Genetics Medicaid Program	Caroline Bey Suzanne Cassidy
3. California State Genetics Program	George Cunningham
4. Washington State Health Department	Robert Fineman Deborah Doyle

Figure 6

Figure 7

Figure 8

Figure 9

THE GROWTH OF CAPITATION		
The 10 states with the fastest growth rates of capitated health plans		
	Percentage of population in capitated plans	**Percentage increase 1990 to 1993**
California	32.9	12.3
Massachusetts	32.7	21.8
Oregon	31.5	18.8
Colorado	21.6	12.5
Connecticut	19.5	14.4
Delaware	19.4	18.0
Maryland	19.4	16.4
New York	19.2	12.1
Pennsylvania	16.3	12.6
New Mexico	16.1	12.9

Source: *The Competitive Edge*, InterStudy, Minneapolis, 1994.

Figure 10

Table 5

OHIO MEDICAID PROVIDER HANDBOOK CHAPTER 3336

Special Genetics Services

Special genetic services are covered as physician services if:

- the genetic services are provided for genetic conditions that usually have serious psychological or medical implications for the individual and the individual's family members;
- the genetic services are prescribed and performed under the supervision of a clinical geneticist (M.D. or D.O.);
- the special genetic services are rendered either:
  - personally by a clinical geneticist; or
  - under the supervision of a clinical geneticist by individuals who meet the criteria established by the "American Board of Medical Genetics" or the "American Board of Genetic Counselors"

Table 6

OHIO MEDICAID PROVIDER HANDBOOK CHAPTER 3336

Reimbursement of Special Genetic Services

The following codes may be billed only if the criteria set forth above has been met and the services are provided in accordance with the guidelines established by the "Ohio Genetic Center Directors."

Code	Description	Fees Hospital	Fees Non-Hospital
X1470	Pedigree construction, initial	$80.00	$100.00
X1471	Pedigree construction, update	20.00	25.00
X1472	Psychosocial genetic assessment, standard	24.85	31.06
X1473	Psychosocial genetic assessment, complex	49.60	62.00
X1474	Medical genetic counseling, initial	40.00	50.00
X1475	Medical genetic counseling, follow-up	20.00	25.00
X1476	Psychosocial genetic couseling, initial	24.85	31.06
X1478	Psychosocial genetic counseling, follow-up	20.00	25.00

A professional and technical component will be recognized for each of the codes listed in this section.

- When the services are provided in a hospital setting, the codes must be billed with the modifier 26.
- When the services are provided in a setting other than a hospital, the services must be billed without any modifiers.

Figure 11

Figure 12

Figure 13

REFERENCE LAB ALLIANCE

Implementation Phases

Phase I:

Establish a regional core of lab capabilities to effectively support the sendout needs of the region's hospitals (completed 12/94).

Phase II:

Link the core entity (logistics, systems, marketing) to the region's acute care/community hospital labs (1/95-12/95) so that testing can be performed on a distributed basis in each hospital lab, while activities such as data collection and contract administration are integrated regionwide.

Phase III:

Collectively approach managed care providers, offering them rapid, professional, cost-effective, hospital-based diagnostic services regionwide (done parallel with Phase II).

Phase IV:

Demonstrate a service which redefines the role and value of the hospital-based lab in the managed care environment (1/96-6/97).

National Coding for Genetic Services

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Billing and reimbursement for genetic services have not been well codified. Fundamental differences in consultation services for complex patients at risk for genetic disorders as compared to other types of patients similarly coded has compromised clinical service reimbursement. Laboratory genetics coding has not kept pace with the rapid changes in technology. In order to increase the flexibility of the existing CPT (Current Procedural Terminology) coding system and to make it more current, the American College of Medical Genetics has proposed an overhaul of the CPT codes used for clinical cytogenetics, clinical biochemical genetics, molecular diagnostics, and genetic counseling.

The national system for reimbursement from public funds is under the Health Care Finance Administration (HCFA). Although HCFA is primarily concerned with Medicare reimbursement, most states and third party payers accept the CPT coding system as an indication of those services which are accepted as part of standard care. Therefore, even though geneticists have not historically been involved in the provision of services to a Medicare population, the CPT codes accepted at this level rapidly spread through the system. CPT codes are developed through the American Medical Association's CPT Advisory Panel. Changes in CPT are incorporated into the HCFA Common Procedure Coding System (HCPCS) of which there are three levels. Level I and II codes are national. The level I codes/modifiers are in CPT-4 and must come from AMA. Level II codes/modifiers are developed by HCFA to supplement CPT-4. Level III codes/modifiers are developed locally by Part B payers and meet the unique needs in service provision at local levels.

Simultaneous with the changes being sought for national coding of genetic services, changes are already evident in the development of a number of successful state-based coding systems which have greatly improved the billing and reimbursement of these services within those states. Once the national CPT codes are in place, efforts will be directed at broadening the service coding systems within other states through the genetics communities within those states.

Not only have the codes themselves been inadequate, recent surveys have demonstrated that genetic service providers are not maximizing their use of the coding systems. The problems were generally ones of underrepresentation of levels of service.

The field of medical genetics will face a number of problems related to transition from fee-for-service to capitated service provision. These include:

- lack of established practice guidelines
- the absence of genetics from contract requirements for Managed Care Organizations (MCOs)
- poor cost analysis data
- limited outcome data

A proposal to update the CPT codes available for genetic testing and counseling services is under review by the AMA CPT Editorial Panel. The types of changes we have proposed are outlined in Table 1, though not by their specific stacked code combinations. Codes that are accepted would be available in 1997.

Table 1

PROPOSAL FOR NEW CPT CODES

I. CYTOGENETICS

a. Fish Testing - Metaphase
   unknown vs. microdeletion/duplication
b. Fish Testing - Interphase
   constitutional vs. cancer
c. Cancer
   analytical code
d. Freezing (short term) for sequential testing
e. Thaw and expansion of established cell lines
f. Interpretation and report (complex cases)

II. MOLECULAR GENETICS

a. Primarily new technologies
   - broaden to nucleic acids
   - distinguish multiplex from singleton assays
   - unknown mutation detection - per each segment
   - sequencing - per each segment
   - protein truncation tests

III. BIOCHEMICAL GENETICS

a. Revision of existing system
b. New subsection for biochemical genetic testing
   - tissue (each)
   - amino acids
   - carnitine/carnitine esters
   - MPS
   - organic acids
   - sugars
   - very long chain fatty acids
   - enzymology
   - interpretation & reporting
   - analytical techniques for quantitative and qualitative assays (e.g., MS/MS, GC/MS, TLC, electrophoresis)

IV. GENETIC COUNSELING

Requests five codes distinguished by time and complexity of service

Managed Care and Its Impact on Genetic Services

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I'm here to report on a conference held last September by PSRGN called "Managed Care and Genetic Services: Translating Needs into Action." The roots of our conference go back to last Spring's ACMG conference, when we heard about the strong concern about managed care and its potential effect on the delivery of genetic services. We also saw individual providers struggling with a wide range of problems from decreased referrals to the loss of choice over which lab tests to order and where to send them. So, PSRGN decided it would be appropriate to hold a conference on the topic to begin to learn about managed care, and figure out how we could address these problems and take advantage of opportunities. We've moved managed care to a high priority in PSRGN, since it doesn't do us any good to develop good educational materials and high quality services if people can no longer gain access to them.

The title of this talk is the impact of managed care on genetics. That's an easy one to address: the impact, as all of our panelists except the managed care representatives stated, has been to seriously disrupt the delivery of high quality, comprehensive, genetic services. Why? The short answer to that question is also easy and well known: Cost. Everything a managed care plan does is motivated by the drive to contain and cut costs, and to a lesser and derivative extent, to streamline the administration of contracts. As Dr. Paul Torrens pointed out in the PSRGN conference overview, healthcare delivery has turned around 180 degrees from a system that was driven by patient's needs and doctor's and technology's ability to meet them, to the current system that is driven by how much payor's and intermediaries, the insurance companies, are willing to pay

Problems

Our panelists, each from their own perspective, produced a list of problems generated by the bad fit between the way managed care goes about cutting costs and geneticists go about delivering quality service. I will touch briefly on each of the major problems, not to be depressing--I hope we've moved past that, but to point out areas where we need to act.

I'll start with the gatekeeper concept. Gatekeepers, in theory and in advertising, are supposed to coordinate a patient's healthcare and to pass the patient on to a specialist when appropriate. In reality, patients are attached to medical centers, not medical doctors, and change plans frequently if they find a less expensive plan. As Dr. Long, the pediatrician on the panel pointed out, referral is discouraged by bureaucratic hoops for approval and financial disincentives, such as report cards that give bad grades to doctors who refer too much. Capitation, also works against referral, since a specialist's fee comes out of the capitation rate, and hence the gatekeeper group's profit. The effects of this, of course, can be misdiagnoses and missed diagnoses, inadequate treatment, and a lack of communication between the geneticist and gatekeeper about new treatments and information about a patient's condition.

A second area of problems was pointed out at our conference by Dr. Marilyn Jones, and I'll call it the contracting problem. As clinical genetics has grown up as a medical field, the model of care that has developed is comprehensive care centers, such as Dr. Jones's Craniofacial clinic. Her clinic includes MD geneticists, genetic counselors, surgeons, dentists, as well as a whole host of ancillary professionals, such as speech therapists, psychologists, and so on. This structure fits rather poorly with the managed care structure of the individual provider contracting for specific services. Furthermore, the potentially enormous amounts of contracts needed to cover services for the team approach to treating the many different genetic conditions creates a bureaucratic nightmare.

A third area of problems is in genetic testing and screening. First, if the health plan authorizes genetic testing at all, the geneticist often has to go through a gatekeeper who will obtain authorization. Aside from the time spent on paperwork needed to justify the test, geneticists have had difficulty in obtaining the results to follow-up with their patients. Second, there's the issue of quality. Many insurance companies contract separately with laboratories to get volume discounts. The provider loses control over which lab to send tests to, and with that, loses the ability to ensure and even know about the quality of the testing. A megalab that makes its money on sodiums and glucoses, doesn't necessarily do a good job on the molecular genetic and cytogenetic tests it throws into the managed care package, and in fact, some do make serious mistakes in their testing. Sometimes these mistakes are caught, other mistakes might not show up for decades. Another issue is interpretation of genetic tests by labs. Several of our panelists reported about patients whose primary care doctors ordered genetic tests, but didn't have the time or expertise to read a long lab report, and consequently made incorrect interpretations.

A fourth area is a bit nebulous, but has to do with genetic information. As Dr. Mike Kaback pointed out, geneticists have been trained to believe that the goal of genetic medicine is to help patients make the most informed decisions that they can for themselves. However, information that isn't tied to an outcome, whether it's a diagnosis of a manifested disease or a treatment, doesn't have any value within the managed care system. It doesn't cut costs, and it isn't always clear how it will improve the lives of enrollees. It then becomes difficult to justify genetic counseling and genetic testing. Another issue raised by genetic information, is that as the genome project maps more of the human genome and links genotypes to phenotypes, geneticists will have more and more power to diagnose, not just rare diseases, but common diseases. As primary care providers take over more of a patient's care, and as more money is at stake in genetic testing, it will no longer be geneticists with their knowledge of the ethical and social implications of testing and screening and training to explain concepts of risk that will be advising a patient whether to be screened for breast cancer or some other disease. Instead it will be managed care administrators and busy primary care providers who have little or no knowledge of the standards carefully developed within the field of genetics. The point is, that with time, genetics will encompass more and more of the range of human diseases, but will require specialized skills, ranging from a working knowledge of molecular genetics to an understanding of the ethical and social implications of genetics. Will geneticists be the providers giving the services requiring this training?

The last major area of problems is genetic discrimination. In the PSRGN region there are existing laws in California, and bills that will soon be proposed in Hawaii, that prohibit an insurance company from

denying or increasing the cost of health insurance based on the result of a genetic test that determines a person is trait positive for a genetic disease. Despite legislation in California, discrimination still occurs. In the U.S. Senate, Senators Kennedy and Kasssebaum have co-sponsored a bill to prohibit the denial of health insurance based on pre-existing conditions. This bill has been put on hold by majority leader Bob Dole at the request of seven anonymous senators. The fact that a bill in the U.S. Senate that has broad bipartisan support can be held up anonymously by seven senators attests to the determination of the insurance industry to cherry pick or screen potentially expensive enrollees to maintain a relatively healthy pool of enrollees to keep costs down.

Opportunities for Action

What can we do about these problems? All of our panelists gave recommendations for action, which I'll call tools to maintain access to quality services. Some of these tools were recommended repeatedly. One of which is the need for guidelines. Guidelines are an explicit way to give the profession's consensus on quality services. Now, many genetic professionals and public health organizations have responded to the need for guidelines, but it should be kept in mind that they'll be most effective when endorsed at the highest levels and become a standard of their own. As these guidelines are developed we can develop concurrent definitions of "medically necessary" services. These would correspond to what the experts, the providers who are actually treating patients, determine, rather than to the restrictive definitions given by the health plans.

Another tool is the referral questionnaire or screening tool, which also sets standards and provides a measure of oversight of a health plan. If an investigation shows that a patient answered a question in such a way that indicates some kind of further action should be taken, and it wasn't taken, this would measure the quality of the plan. When a template for action is included in the questionnaire for the primary care physician, this also aids him or her to make decisions. MSRGN has developed such a questionnaire, and PSRGN is adopting this model.

Another tool is education; education of primary care providers, education of medical directors of health plans, education of the public through the media.

Finally, we were called upon repeatedly to identify and document problems that arise with managed care plans. To this end, PSRGN has started to distribute a complaint form to providers and consumers, which will be collected and reviewed periodically. Other regions are conducting surveys of providers to obtain this information.

In the next part of my presentation, I'd like to discuss the levels at which we can apply these and other tools.

Government Regulation-- The first level I'll talk about is government regulation. There isn't very much oversight of managed care health plans from either the federal or state governments, although that is changing. The movement of healthcare administration and oversight seems to be away from governmental centralization, that is from the federal government towards the state governments, and

from state governments into private plans. We can see this through the efforts of members of Congress to gut the Medicaid and Medicare programs, and shift them to the states through block grants. Therefore, the ten CORN regions would be most effective in tracking regulation at the state levels; however, they can use tools developed at the highest organizational levels in the genetics community, such as CORN, ACMG, ASHG, and NSGC. Using the CORN guidelines as a standard of quality for medicare managed care is an example of this. In PSRGN we're working with California Medi-Cal Managed Care to introduce standards of quality. We're also working with legislators, such as Senator Johnston who spoke at our conference. Since the conference Senator Johnston has put together a Select Committee on Genetics and Public Policy to begin to educate other members of the California Senate about genetics and to sponsor legislation.

In the legal arena, lawyers are focusing on contract language, since there are very few laws in place. The lawyers on our panel reported that the courts are focusing on the term "medically necessary" when ruling on healthcare cases, but have not seen any clear pattern in one direction or another in the rulings.

A specific area I'd like to mention that is begging for governmental regulation are the so called provider "gag rules." These are rules that prohibit providers from discussing problems their patients are having with the health plan the provider has contracted with, which effectively prevents providers from advocating on behalf of their patients.

Managed Care Plans What about the level of the managed care plans themselves? If we accept the fact that the managed care plans are writing their own rules, then we need to look at what they are using to evaluate the quality of their plans and how they decide which services to cover. On the one hand, it's important to keep in mind that we don't have time on our sides in the sense that every day major decisions are being made about coverage, etc. On the other hand, the field is fiercely competitive, and as time goes on, it will become more and more apparent where the big problems are in managed care.

So, what are the areas where we can influence the plans and how can we work with them?

First, is education. There seems to be at least some, no telling how much, ignorance about genetic services within these plans. When we were deciding on speakers, several medical directors were recommended to us by a former California Director of Health Services. The medical director and managed care board member who spoke at our conference advocated talking to medical directors and trying to educate them, although they warned us it wouldn't be easy to be heard.

Another way to work with managed care plans is through their Quality Assurance panels. Many managed care plans are looking for evidence-based outcome studies and cost-benefit analyses. While we can give them these analyses for the common diseases that are currently screened through newborn screening programs or prenatal detection, this becomes much more difficult for rarer diseases or diseases for which genetics, as a new field of medicine, doesn't have much data. Genetics has special problems in terms of small numbers and the need to follow a patient for a long period of time to get outcome data. We need to support expert opinions as an interim alternative.

Payers-- Another target genetics can approach is the payer. If you recall the first overhead on the dynamics of healthcare, payers are at the top, and are highly motivated by cost. The other important thing to remember about payers, is that right now there is a movement towards their consolidation into large purchasing cooperatives, such as the Pacific Business Group in California. They pay for three and a half million covered lives, which gives them the leverage to negotiate fees and the services they'll cover. Unfortunately, the burden of cost has been shifted to smaller, unorganized businesses and individuals, who have to pay higher fees. But this is another group to approach with guidelines and education. They also may be more open to arguments relying on the preventive nature of genetic care, since they will be responsible for paying for their beneficiaries for longer than one season or two seasons.

Consumers--One of our speakers, the child advocacy lawyer Elizabeth Jameson, stressed that child advocacy has been in disarray since the defeat of the Clinton Plan for Healthcare reform and that consumers have few protections in the new system, except litigation. Other speakers pointed out that consumers are at the bottom of the feeding chain; they don't have a lot of power, they're receiving less services and lower quality care, or are completely shut out of the healthcare system. However, there are a few options that consumers can pursue. One option is to use the grievance system of the health plan and the government and to document the grievance process. Another way to support consumers is to provide them with information beyond the cost of plans to aide them in their choice of plans--information such as report cards of health plans and criteria for choosing a plan. The option of last resort, but certainly an effective one both for the individual and for shaping policy is litigation. We also need to be clearly supportive of consumer advocacy organizations.

Providers At the primary care provider level, education is the strongest option. CORN is sponsoring a primary care provider education workshop next month to review primary care provider education by SPRANS (Special Projects of Regional and National Significance) grantees and to develop recommendations. The Human Genome Project has funding to identify past or current programs designed to improve health care providers' understanding of genetics and incorporate genetic services into primary care. The Alliance for Genetic Support Groups is beginning an educational project in the nation's medical schools. These, and all of the CORN region's primary care programs are some of the major efforts in the country to educate primary care providers about genetics.

Options for genetics providers suggested at the conference involve organizing themselves into fiscal entities. Dr. Mike Kaback suggested that geneticists should form consortiums and contract out as a group to managed care plans. He also pointed out that one of the problems with this approach is that not all geneticists will be able to be part of a consortium. How do you make the decision about who to include? Marilyn Jones thought that the Kaiser model would work best for genetics. It cuts out multiple layers of contracting and the plan makes coverage decisions on a wholesale policy basis, rather than looking at each case.

In closing, I'd like to point out that despite our skepticism of managed care's commitment to quality healthcare services, we should make every effort to work with them and allow them to demonstrate this commitment.

The Impact of the Current Legislative Climate on Genetic Services

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INTRODUCTION

This presentation will be divided into two sections, both having a direct impact on the scope and provision of genetic services. The first deals with the current Congressional fiscal climate, i.e., the process of negotiating a balanced budget by the year 2002; and the second dealing with the specific legislative initiatives having direct implications for genetic services.

The legislative drive for a balanced budget and the concomitant "downsizing" of government to its more "svelte" conformation are direct results of the 1994 Congressional election. Regarding our own specific area of interest, the spotlight became focused on the ever-increasing costs of health care and related issues through the prolonged deliberations on health care reform in1993-94 culminating in the Health Security Act of 1994. Although never enacted, that legislation and the discussions leading up to it detailed the complexity of US health care which interweaves such diverse areas as the insurance industry, the medical research community, the professional educational establishment, a host of welfare programs, the Immigration and Naturalization Service, and many governmental regulatory and social service agencies at the federal, state, and local levels.

The salient feature of this exercise was to clearly identify the magnitude and intricacies of providing health care services and the cost to the Federal government. The trust funds providing the monetary underpinning for mandated social programs, of which Medicare and Medicaid are by far the largest would become insolvent by 2002 if the rate of annualized increased spending were not curtailed. At the same time, in the private arena, after more than a decade of "tooling-up", the effort to contain the ever-increasing costs of medical care, primarily propelled by the managed care industry, reached its peak activity. The coincidence of both public and private initiatives to restructure the US health care delivery system defines the situation in which we currently find ourselves.

THE BUDGETARY ENVIRONMENT

Several major contributors to the present status include:

1. **The Medicare/Medicaid Debate** — In the attempt to balance the Federal budget, no single issue is more important. These two entitlement programs provide the most accessible targets offering the greatest opportunity for reduction in national spending, with initial Congressional action cutting $270 billion from the former and $182 from the latter. Estimates indicate that such action in the Senate will force hospitals to reduce Medicare-reimbursed services by $86 billion, while the House action would lead to an additional $76 billion loss of services. Projected Medicaid reductions would add tens of billions of dollars loss in covered services. These figures are still under debate by the legislative and executive branches and the final size of any reductions and the magnitude of any actual "savings" to be realized are unclear. The philosophical change of converting the Medicaid program from a Federal

mandate to a "bloc grant", administered at the State level, raises many questions concerning efficiency and accountability for the actual expenditure of funds so earmarked.

However, the impact of these ultimate reductions reaches well beyond the programs themselves and directly affects the operation of academic health centers through its effect on training. A significant portion of trainee support is, in actuality, provided by Medicare patient care funding through direct and indirect contributions to medical education (DME & IME) payments. Current legislation directs annual reductions with ultimate elimination of such support over a four year period. In addition to expenditure reduction, a secondary effect of this proposal is to reduce the number of residents being trained in line with projected personnel needs for Medicine. Without continued support for training and reduced Medicaid income, teaching institutions would not be competitive with those hospitals that do not assume the additional responsibilities of education, indigent care and research. An initiative to address this inequity has been included in the House "Medicare Preservation Act" as the "Teaching Hospital and Graduate Medical Education Trust Fund" which has been supported by many stakeholders as a positive step toward building a shared responsibility approach for supporting the tripartite mission of academic health centers. These deliberations have a direct effect on the provision of genetic services and training of clinical geneticists. With the recent recognition of the American Board of Medical Genetics as the newest of Specialty Board with its independent Residency Review Committee and the admission of the American College of Medical Genetics to the Service and Specialist Society and its recommended entry into the American Medical Association (AMA) House of Delegates, we have "arrived" on the scene of organized medicine. As such, our clinical training programs must adapt to national norms, including renaming trainees as Residents, whose funding will be affected by the Medicare/Medicaid debate.

2. **Managed Health Care** — Although not directly attributable to legislative activity, the effect of the penetration of managed health care plans on the provision of genetic services cannot be overlooked. As a result, a basic transformation in the way service provision is organized, delivered and, most importantly, financed is occurring. The driving force of the new order is the supreme position occupied by "economic" considerations. Undivided attention to the "bottom line" while providing services to ever-increasing numbers of patients in order to capitalize on economies of scale are central to the new fiscal responsibility. This is best achieved through capitation schemes in which the provider shares in the assumption of risk with the primary payer. In addition, greater emphasis is being placed on preventive, ambulatory primary-care, in an attempt to minimize dependence on higher cost hospital-based facilities. Such activity is to the detriment of specialists and particularly affects geneticists since they are:

a. subspecialists dealing with a very delineated area of medicine
b. in the main, associated with academic health centers
c. not able, generally, to compete successfully for "all-inclusive" capitated contracts.

In isolated exceptions, some health maintenance organizations (HMOs) have "broken out" genetic packages for “comprehensive genetic care” plans, but their success has not, as yet, undergone qualitative or financial evaluation.

The characteristically unique quality of the team approach to comprehensive genetic services is seriously threatened by managed health care since the integration of clinical, laboratory, counseling and social service patient support may be visualized as too expensive by including a large number of sub-specialists. This is most obvious with respect to laboratory diagnostics which might, as a stand-alone financial venture, prove somewhat more successful in the new economy. However, such labs must be competitive in a market which includes many large for-profit enterprises. This philosophy cannot help but weaken the concept of the comprehensive program, whose rationale for existence is providing integrated genetic care.

3. **Restructuring of Academic Health Centers** — These institutions are facing serious threats as they deal with the enormous challenge of trying to accomplish more with less. Their survival and future depend solely on their willingness to commit to flexibility. Changes currently under consideration for implementation include a greater emphasis on primary care, organized in a distributed, rather than a concentrated, fashion. The construction of geographically disseminated networks, providing outpatient services in numerous, patient-convenient locales, further de-emphasizes the importance of "the hospital". The necessary adoption of a fiscally responsible approach, along with the mimicking of, and simultaneous competition with, managed care practices has reduced the number and altered the distribution of specialists needed to cover such networks. Due to the relative rarity of genetic disease, the number of "covered lives" needed to support genetic specialists (the capitation concept) is exceedingly large.

4. **Training** — In keeping with the general restructuring underway according to the projected workforce needs for medicine, a recent report from the Pew Health Professions Commission has recommended reducing the number of medical schools by 20 percent and the total US medical school enrollment by 20-25%, as well as placing limits on the number of graduate medical education positions for international medical graduates. This report raises a controversial issue regarding the limitation of opportunity for pursuit of a medical career. In human/medical genetics, several needs assessment surveys have occurred projecting workforce requirements made for various areas (counselors, cytogeneticists). Currently, a comprehensive, discipline-wide study is underway under the aegis of the Council of Regional Networks for Genetic Services (CORN) and the American Society of Human Genetics (ASHG). Upon completion, this study may provide an assessment of the current situation and permit future needs requirements in line with the changing scene. There is an unsubstantiated feeling that we are in an "overproduction" phase of training genetic specialists, both MD and PhD practitioners. However, until the reliable information becomes available, this apparent surplus of geneticists remains unconfirmed. However, due to the impending reduction in training support, either from research or training grants *per se* or Medicare reform, coupled with a probable diminished trainee demand, we must realize that such activity is liable to assume a less central position in many programs.

5. **Research** — As Government spending in many areas is dwindling, the public's attention has been focused on the effects of suggested cuts in large "entitlement" programs as well as the anticipated benefits of a "tax-cut". Less noticed are reductions in programs which also have a profound significance to the public, although in an indirect manner. Regardless of which balanced budget proposal is considered (either the Congressional or Executive) approximately one-third of the $40 billion allocated

annually for non-Defense research and development will disappear. The main goal of programs supported by these funds is the acquisition of new knowledge for the public good. As a result some entire departments and programs face immediate cuts - or even elimination (e.g., the Department of Commerce, NASA, Environmental Protection Agency (EPA), and the Office of Technology Assessment). With specific relevance to health related programs, both the National Institute for Occupational Safety and Health (NIOSH) and the Agency for Health Care Policy and Research are in jeopardy due to budgetary cuts that imperil their ability to function.

Perhaps most significant is the budget projection for the National Institutes of Health (NIH). Although the most recent Congressional action suggested increases for FY1996, to date this legislation is currently being held in abeyance due to the lack of agreement on the Appropriation Bill for the Department of Health and Human Services. Fortunately, the most recent "continuing resolution" provides funding for the remainder of FY96 at the House approved level of $11.939 billion, which represents a 5.7% increase over FY95. This is but a temporary measure and due to the continuing budgetary negotiations, it is very difficult to predict what the NIH's budgetary requests for FY97 might be. However, that request will undoubtedly reflect the principles of the FY96 request, i.e., minimizing the earmarking of specific projects while emphasizing certain areas of research, including genetics, across the institutes. Nonetheless, one must assume a sanguine approach to the longer view which includes the projected impact of a balanced budget on discretionary (non-mandated) spending.

Reauthorization for the NIH, a process which recurs every three to five years, is on the agenda for the current session of the 104th Congress. The inclusion in the NIH program of several research initiatives (e.g., fetal tissue and embryo research, gene therapy, germline manipulation) however pose difficult philosophical/political dilemmas which may affect ultimate action on this legislation.

The confluence of the above factors create a new milieu for the provision of genetic services. A critical issue that must be confronted is the possible future change in venue for the provision of clinical services and, central to this problem is the transmission of information relevant to the patient and family. With the impending shift of service to a distributed "primary care" format, the “generalist” practitioner will have to assume much of the role of the current genetics care provider. This poses, perhaps, the most serious challenge facing the profession today: that of educating general practitioners in the complexities of modern human/medical genetics. On the laboratory side, competition for market share is assuming a greater proportion of the activity of academic diagnostic laboratories. To remain competitive with commercial laboratories, active marketing efforts and price restructuring must be undertaken at the expense of time currently devoted to training and research. Creative solutions to these two problems are essential for the maintenance of excellence and quality in the provision of genetic services.

LEGISLATIVE INITIATIVES

Budgetary and Appropriations Considerations: Perhaps the greatest influence on the provision of genetic services will emanate not from the effect of individual pieces of legislation, but from the annual processes of budget development and appropriation of funds for governmental programs. The current debate, demonstrating the deep differences in political philosophy in approaching a balanced budget, a

principle agreed to by both parties, will undoubtedly affect, in a most significant manner, the health care delivery system in the country.

The most vulnerable programs in this process, by the sheer size of the monetary impact, are Medicare, Medicaid and various Welfare initiatives which together provide not only most of the health-care and social services, albeit to different constituent populations, but also provide the largest component of non-defense government spending, and the most likely targets for budget reduction. Although Medicare is earmarked for health care of older Americans, changes in structure and funding of this program will have both direct and indirect effects on genetic services. Until quite recently, genetic services have essentially concentrated on pediatric problems. The almost daily advances in the elucidation of the more common, adult-onset diseases (neoplasia, diabetes, neurological conditions) will force a refocussing of efforts on the Medicare population, but with possibly reduced support for such services. Similarly, reductions in programs to aid the poor and disadvantaged (i.e., welfare and Medicaid), will further reduce the level of support for these populations, the traditional recipients of genetic services. The desire to shift both Medicare and Medicaid beneficiaries into managed care plans will further emphasize the generalist/specialist schism with its negative impact on the provision of specialty and subspecialty services. Moreover, any reduction in Medicare funding will almost immediately be reflected in educational efforts, through the direct and indirect support of graduate medical training, as discussed above.

Although a modicum of funding for health related issues can be found in various of the thirteen appropriation bills which normally fund the Federal government, the vast amount of support is derived from the Labor/Health Human Services/Education appropriation, currently stalled in the Senate. Particularly germane to genetic services are the NIH and Maternal and Child Health Bureau (MCHB) budgets, included in the HHS component of this bill. The Genetic Services Branch of the MCHB contributes perhaps the single largest amount of funding directly in support of genetic services. Although, only a few specific HHS programs (NIH, CDC) have been funded for the remainder of this fiscal year under a continuing resolution (CR), the Maternal and Child Health Bureau is working under short-term CR's essentially at the FY95 level. Additionally, since many of the diagnostic laboratory procedures needed for the support of clinical genetic services are still performed in academic research laboratories, such activities may also be affected by reduced funding. The outcome for NIH this year is extraordinary given the current fiscal environment. However, how this will play out in future requests remains to be seen.

Specific Legislation: A number of individual bills, dealing with widely different topics and which will have a definite impact on the delivery of health care services, are currently working their way through the legislative process. The direct implication of some of these efforts may not be obvious, but ultimately will influence access, timeliness, and patient protection in the provision of genetic services.

1. **Food and Drug Administration (FDA) Performance and Accountability Act of 1995 (S.1477)** — This bill, introduced by Sen. Nancy Kassebaum provides for comprehensive legislation that will reform the role of the FDA in the testing and review of new drugs and medical devices. Such action is

necessary since, over the years the agency's requirements for clinical testing and its premarket reviews of new products have grown increasingly complex and expensive. On average, it takes approximately 12 years to bring a new drug to market at a cost approaching $359 million.

Specific sections of the bill address:

a. emphasizing FDA's primary mission in facilitating the rapid and efficient development and availability of safe and effective products that will benefit the public

b. clearly delineating and strengthening the statutory deadline of 180 days which must be met by the agency in drug approval. Current time periods for review completion for new devices approaches 649 days and new drugs 570 days. The bill requires the Commissioner to report annually on the agency's performance in meeting deadlines and if not in compliance, to contract with outside experts for reviews.

c. ensuring that individuals affected with life threatening diseases will have access to new therapies by expanding "compassionate access" to new drugs and medical devices

d. establishing collaborative clinical testing and review processes by requiring the agency to meet with companies early on and throughout clinical trials to establish and maintain design and minimize changing parameters once the protocol is initiated

e. providing the FDA with the statutory flexibility to modify its clinical testing and product review policies; for example, basing approval on one well-designed clinical trial rather than the "two or more clinical studies"

The direct effect on genetic services of such reform will be in the more rapid availability of new drugs and treatments as they are developed. Additionally, broadening of "compassionate access" to experimental drugs and treatments will significantly expand access by that population of patients affected with life threatening diseases.

2. **Medical Technology, Public Health, and Innovation Act of 1995 (S. 1369)** — This is a second bill (introduced by Sen. Paul Wellstone) which addresses FDA reform with specific emphasis on improving the timeliness, predictability, and effectiveness of the review process for medical devices.

It would require:

a. the use of nationally- and internationally-recognized performance standards, where appropriate, to determine safety and effectiveness of "breakthrough" devices

b. regular, periodic communication between industry and FDA during the premarket approval process for timely identification of application deficiencies and status updates during review and annual publication of progress made in implementing program management improvements

c. improved focus of the premarket approval (PMA) process and exemption of class I and II devices from PMA supplements and 510(k) applications with presentation of appropriate supporting documentation by the manufacturer

d. improvement of the investigational device exemption process by joint development of clinical trial protocols, acceptance of retrospective and historical evaluative data, allowing device changes during the study without additional approval, providing patient safety is not affected

This bill is a work in progress and is currently undergoing further development. Its most direct effect on genetic services is obvious since, at present, all DNA probes used diagnostically are classified as Type III medical devices which must undergo extensive clinical testing and a PMA process. This is a very time consuming and expensive procedure, and based on the limited market due to the relative rarity of individual genetic conditions for which these reagents have been developed, manufacturers are not applying for FDA approval. As a result, they do not have approval for clinical use and must be labeled as "investigational use only". Such classification, in many cases, diminishes the possibility for third party reimbursement, particularly Medicaid, and thereby increases the ultimate cost of the test to the diagnostic laboratory. An attempt is being made to add a new section to these FDA reform bills covering *in vitro* diagnostics, including DNA probes. A reclassification of such devices to Classes I and II not requiring PMA, thereby streamlining the FDA approval process considerably, would be very advantageous.

Several bills in both the Senate and the House deal with the protection of privacy and confidentiality of medical information, in general, and genetic information, in particular.

3. **Medical Confidentiality Act of 1995 (S.1360)** — This bill attempts to establish uniform privacy protection at the Federal level for personally identifiable medical information since state laws are nonexistent or, in many cases, inadequate. Currently, no comprehensive protection for such information exists. This legislation calls for Federal safeguards for medical records, whether in paper or electronic form, and is designed to provide physicians, hospitals, insurance companies, managed care companies and others that have access to such records with clear Federal rules governing when and to whom they may disclose health related information. With the rapid growth, development and expansion of electronic data bases, the potential for abuse of the information increases.

The bill defines the protected information as "any health-related information created or received by a health information trustee that relates to an individual's past, present or future physical or mental health

or condition, care or payment and can identify the individual". A "health information trustee" means "a health care provider, health plan, health oversight agency, health researcher, public health authority, employer, insurer, school or university, or health information service insofar as it creates, receives, obtains, maintains, uses, or transmits protected health information".

The main provisions of the bill include:

a. the individual's right to access his/her own information

b. prevents all health care trustees from disclosing protected information without authorization from the individual with certain exemptions including--

   1. emergency circumstances necessary to protect the health or safety of the individual from serious, imminent harm

   2. investigations by a health oversight agency, investigations of certain legal actions involving receipt or payment of health care or a fraudulent claim, investigations of a public health authority, IRB approved health research projects, judicial and administrative purposes, law and non- law enforcement subpoenas and warrants

c. civil and criminal and civil sanctions, penalties and actions for violations of the Act

d. preemptions of existing state laws except those dealing with mental health and substance abuse in cases in which the state law is more stringent.

During the public hearing on this bill (11/14/95) concerns were raised from several sources (ACLU, the Consumer Project on Technology, American Hospital Association, Center for Democracy & Technology) and those seeking exemption for specific types of information (e.g., psychiatric data [American Psychiatric Association, Coalition for Patient's Rights] and AIDS status [AIDS Action Council]). Additionally, representatives of the health information industry (American Health Information Management Association, Association for Electronic Health Care Transactions) protested being classified as "health information trustees" since they merely transmit the data electronically without actual "access" to it. This is a very broad-based bill which will undoubtedly be debated widely before final action is taken.

4. **Genetic Privacy and Nondiscrimination Act of 1995 (S.1416)** — Results from recent unprecedented scientific breakthroughs have provided genetic information, both retrospective and predictive, which is of immeasurable importance regarding an individual's current and future health status. At present, such genetic information is used primarily by patients and their physicians to provide health related risk assessment. However, exploitation of this very same information has the significant potential for abuse. This bill, introduced by Senators Mark Hatfield and Connie Mack, will help protect citizens from improper use of genetic information and discrimination by insurers and employers. It is modeled on the Genetic Privacy Act recently passed by the Oregon State Legislature and responds to recommendations of the Human Genome Project's ELSI Working Group and The National Action Plan on Breast Cancer. The bill establishes limitations with respect to disclosure and use of genetic

information, and defines the rights of those whose information has been disclosed with the goal of balancing the need to protect the rights of the individual against society's interests. Genetic information is defined as "information about genes, gene products, or inherited characteristics that may derive from an individual or a family member."

Specifically, provisions of the bill would:

a. prohibit disclosure of genetic information by anyone without the specific written authorization of the individual. This disclosure provision could apply to health care professionals, health care institutions, laboratories, researchers, employers, insurers, and law enforcement officials. The written authorization must include a description of the information being disclosed, the name of the individual or entity to whom the information is being provided and the purpose of the disclosure. This provision preserves the individual's ability to control the disclosure of his or her genetic information. Exceptions to this provision are for the purposes of a criminal or death investigation, specific orders of Federal or State courts for civil actions, paternity establishment, specific authorization by the individual, genetic information relating to a decedent for the medical diagnosis of blood relatives, or identification of bodies.

b. prohibit employers from seeking to obtain or use genetic information or require a genetic test of an employee or prospective employee in order to discriminate against that person. It reinforces the Equal Employment Opportunity Commission's (EEOC) official guidance on the definition of "disability" and reiterates that protection under the Americans with Disabilities Act extends to discrimination based on unfair use of genetic information. It makes clear that such practice would be prohibited under Federal law.

c. prohibit health insurers from using genetic information to reject, deny, limit, cancel, refuse to renew, increase rates, or otherwise affect health insurance. This provision will provide much-needed assurance to individuals with preexisting conditions and will ensure that they will not risk losing health insurance coverage when most needed. Such action is in concert with changes under consideration in the health insurance and preexisting condition exclusion included in the Health Insurance Reform Act of 1995 (S. 1028) introduced by Sen. Nancy Kassebaum.

d. require the National Bioethics Advisory Commission to submit to Congress their recommendations on further protections for the collection, storage and use of DNA samples and genetic information obtained from those samples as well as establishment of appropriate standards for the acquisition and retention of genetic information. This provision is intended to ensure that the social consequences of genome research are considered as the technology develops and not *post facto*.

This piece of legislation is considered as a first step which addresses the most pressing concerns surrounding genetic testing and the disclosure of genetic information as it relates to discrimination in employment and health insurance practices. It was introduced to encourage the development of new

initiatives in medical research but not at the expense of patient privacy. The bill has been read twice and was referred to the Labor and Human Resources Committee.

In the House of Representatives, Congressman Cliff Stearns has introduced identical legislation which is identified as H.R. 2690 and has been referred to the Commerce Committee.

5. **Health Insurance Reform Act of 1995 (S. 1028)** — This bill would reform the manner in which health insurance companies sell policies and would provide increased access to health care benefits, provide increased portability of health care benefits, increase the purchasing power of individuals and small employers and includes several other related health insurance issues. This legislation was introduced by Sen. Nancy Kassebaum and currently has 25 cosponsors representing both parties. It was referred to the Labor and Human Resources Committee and underwent two public hearings in July 1995, followed by committee consideration, "mark-up" and a committee report (no. 104-156). The bill has been released by the committee and placed on the Senate Legislative Calendar to be debated in this current session.

General considerations of the bill include the prohibition of health insurers from denying coverage based on health status, medical condition, claims experience, receipt of health care, medical history, disability, or evidence of insurability. It insures accessibility to health insurance even with change of employment (portability), the existence of preexisting conditions (with a 12-month preexisting condition limitation). Protections of the legislation extend to self-insured ERISA plans, to individuals leaving group coverage, and to policies offered to large and medium-sized employers. Its provisions do not supersede state laws which provide "stronger" protections. Although it deals with accessibility and portability, the bill does not address ratings, which is left to the states. Finally, it does provide for a study to make recommendations concerning the establishment of standards limiting variation in premiums, if needed.

Of interest, from the our perspective, is how genetic information is dealt with. Under the section headed "Guaranteed availability and nondiscrimination in the group market", it was hoped to prohibit coverage discrimination based on genetic information. "Genetic information" is defined as "information about genes, gene products, or inherited characteristics of an individual covered under the terms of a plan or about his or her family members...." This was not included in the legislative language *per se*, but the topic is addressed in the committee report which states "the provisions of the bill forbidding group health plans and individual health plans from discriminating based on health status and medical history should also be read to prohibit such plans from establishing eligibility, enrollment, continuation, or premium contribution requirements based on genetic information". While such report language is very helpful in interpreting the sense of the legislation, it is only instructive to administrators and the courts but does not carry the same force and effect as law. The bill does not prevent companies from basing premiums on medical information which could put coverage beyond the reach of many individuals.

In the House of Representatives, the "Genetic Information Nondiscrimination in Health Insurance Act of legislation has been introduced by Rep. Louise Slaughter and 25 cosponsors. In addition to being introduced as a free-standing bill (H.R. 2748), the legislation is also part of the "Women's Health Equity

Act". This bill would prohibit insurance providers from denying or canceling coverage, or varying premiums, terms, or conditions for health insurance coverage on the basis of genetic information or a request for genetic services.

Sen. Diane Feinstein is currently working on legislation that is expected to address these same issues. This bill is still in draft form and currently undergoing revisions, but should be introduced shortly.

Informed Consent and the Use of Archived Tissue Samples

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Abstract

Collections of archived tissue samples are attractive sources of material for population-based studies in genetics. Appropriate use of these collections may rest on the nature of consent obtained from source persons at the time the tissues are collected. Depending on the legal and technical circumstances, consent of source persons may be unnecessary, or it may be explicitly required, or it could be part of a blanket consent for subsequent use. If archived samples are used anonymously, investigators should recognize degrees of "anonymity" that may bear on the rights of source persons. Investigators in human and medical genetics should also consider the possible obligation to inform source persons about the existence and/or the nature of new information that is generated by the use of archived samples. A forthright process of informed consent will provide maximum respect for the rights and decisional authority of source persons as well as maximum protection *and* flexibility for investigators in human and medical genetics.

Introduction

The rapid expansion of technologies in modern molecular genetics has raised a number of serious questions about appropriate interactions between scientific and medical personnel, on the one hand, and the individuals who participate as subjects in genetic testing and research, on the other. Geneticists have been quick to realize that large collections of tissue samples may be immensely valuable in research on gene structure and in research on gene frequencies in the populations of origin. Particularly tempting are the collections of blood spots that are gathered from the newborn population as part of state-funded programs to detect and treat phenylketonuria, sickle cell anemia, congenital hypothyroidism, and a few other early onset diseases. About 4 million newborns are screened in public programs each year; so newborn screening creates an immense set of samples that could be extremely useful in answering questions in human and medical genetics.

The genetics community has acknowledged the value of these collections in proposed research projects, but this enthusiasm has been tempered by skepticism on the part of some about the ethical and legal implications of using stored samples. Several investigators have raised questions that require consideration of appropriate uses of archived samples in genetics research. One major concern is the issue of informed consent in newborn screening, and the fact that there are very few provisions for obtaining the permission of parents for the participation of newborns in screening programs and for future use of screening samples in genetics research. Some research scientists have argued that the consent of parents is unnecessary if the stored samples are used "anonymously" in various research projects, although there is presently no consensus about what actually constitutes anonymous use. Also, some geneticists have voiced concern about the interests of individuals in genetic information that may be discovered in the future and that could have an impact on the lives of the source persons (Clayton, et al., 1995).

The use of samples that are collected in population-based screening programs is of particular interest because these programs are founded on concern for public health. If the genetics community continues to seek access to these collections of biological samples, three important issues deserve careful study and analysis. The first issue is defining any principles of informed consent that should be incorporated into screening programs. If collections of archived samples are used in research, with or without identifiers or identification codes, the second concern is defining the conditions for "anonymous" use of archived tissue samples. A third question focuses on the possible obligation of the geneticist or researcher to convey new genetic information to persons who are the sources of archived tissue samples. Finally, these concerns can be readily incorporated into a protocol for consent that will take all of these issues into consideration.

Principles of Informed Consent

The legal Doctrine of Informed Consent has developed over the course of this century in two separate, but related, contexts, both of which have acknowledged the moral principle of personal autonomy as the foundation of interactions between medical professionals and their patients or subjects (Faden and Beauchamp, 1986). One type of informed consent inheres in the physician-patient relationship, while the second derives from the interests of biomedical research scientists in elucidating the origins and processes of human diseases and disorders.

In the context of the physician-patient relationship, patients enjoy an acknowledged right, derived from the moral principle of personal autonomy, to give informed consent for medical treatment and surgical procedures. The evolution of this right and the criteria for obtaining informed consent have followed a steady and deliberate course over the course of this century. From tenuous beginnings in individual malpractice cases, the process and content of informed consent is now a matter of both case law as well as statutory law in many states (Pelias, 1991).

Similarly, the concept of informed consent for participation in biomedical research has been at best a rudimentary idea over much of this century. However, the revelation of the atrocities carried out before and during World War II generated the Nuremberg Code and the Declaration of Helsinki, both of which acknowledged the rights of individuals and the value of voluntary, informed participation in health care research (Appelbaum et al., 1987). In spite of the acknowledgment and adoption of these principles by the biomedical community, however, research and experimentation without the consent of human subjects has continued in the United States, some of it into the 1970's and beyond. Nevertheless, public and professional disapproval of the tactics and methods of some researchers has resulted in cooperation of the federal government and the scientific community in creating an elaborate structure for regulating and approving biomedical research with human beings. This system of federal regulations and institutional review procedures has the specific goals of shielding human subjects from exploitation and unnecessary risk.

About 30 years ago the progress of genetic technology and the treatment of genetic disease was boosted significantly with the discovery of an inexpensive, reliable test for detecting phenylketonuria and the inception of the era of newborn screening. Because of the immense benefits to both individual children

and to the public fisc, many states initiated programs for screening the newborn population and for assisting children and families who needed the benefits of dietary or medical management (Newborn Screening Committee, 1994). While some consideration was directed to emerging notions of informed consent, both the medical and legislative communities emphasized the great benefits of newborn screening and addressed issues of informed consent secondarily, if at all (Andrews, et al., 1994).

More recently, state-funded programs have approached the idea of informed consent in newborn screening from several perspectives that give more or less consideration to parental autonomy and the right of parents to make decisions on behalf of their minor children. However, provisions for informed consent vary considerably among the state jurisdictions. At one extreme are two jurisdictions that require parental consent before any samples are collected from the newborn infant. At the other extreme are two states that have such rigid mandates that parents are not allowed to refuse even on the basis of their religious beliefs, and two states that provide criminal penalties for parents who refuse to allow their infants to be tested. Most states, however, do allow parents to refuse testing, based on their religious beliefs, and most states also provide some procedure for obtaining parental consent, even if consent is sought only after blood samples have been collected from the infant. What is still lacking in protocols for informed consent in newborn screening is explicit permission for future use of samples that are stored away after newborn testing is complete.

The continuing lack of uniformity among the various states in legislative provisions for informed consent in newborn screening underscores the importance of recommendations from national or federal sources. In response to the new implications of using collections of tissue samples for research in human and medical genetics, the issues of informed consent are now the subject of considerable attention in the community of genetics professionals, including medical practitioners, research scientists, and others who have special expertise in genetics and health care and in the legal and ethical implications of modern medical genetics (Andrews, et al., 1994; American College of Medical Genetics (ACMG) Storage of Genetics Materials Committee, 1995; American Society of Human Genetics (ASHG) Ad Hoc Committee on Individual Identification by DNA Analysis, 1990). What is still missing from these professional deliberations and recommendations is a model protocol for informing parents about the newborn screening process and the implications of future use of stored samples.

Definitions of Anonymity

While many investigators acknowledge the current dilemmas of informed consent in newborn screening, the movement to gain access to archived tissue samples continues to gain support in the scientific community. A number of investigators have suggested that all archived collections of samples should be available to researchers who agree to use the samples "anonymously." Investigators who are formulating guidelines for the use of archived samples have distinguished between retrospective studies based on using old collections of samples and prospective studies based on using new or future collections of samples. A distinction is also drawn between anonymous samples that have no personal identifiers and "anonymized" samples, from which personal identifiers have been removed. Some investigators have suggested that informed consent should not be necessary either in retrospective

studies using anonymized samples, or in prospective studies using anonymous or anonymized samples. The final deliberations and recommendations of these investigators are forthcoming (McCabe, 1996).

One continuing difficulty in permitting the use of archived samples lies in potential confusion over the definition and implications of the words "anonymous" and "anonymized." The major stumbling block in defining anonymity is how one should - or must - separate personal identifiers from tissue specimens. This confusion permits several interpretations of "anonymous" use:

> (1) One level of anonymity might involve the separation of identifiers from coded samples in a single laboratory, with limited access to information that would permit personal identification of any one sample.
>
> (2) A second level of anonymity would be achieved with identifiers filed in one laboratory, or in state archives, and coded samples used in other institutions.
>
> (3) A third level of anonymity could be achieved if samples are used in various institutions without codes or identifiers.
>
> (4) A fourth level of anonymity would entail the destruction of identifiers prior to any further use of archived samples.

The first and second arrangements would permit identification of the source person if newly developed genetic information could be of importance to the source person. The third and fourth levels, on the other hand, would involve irreversible separation of codes and identifiers from samples, a procedure that would preclude subsequent identification of source persons, even when new genetic information could have a significant impact on how the source person might wish to plan his or her life.

The implications of future use of archived samples include the content of informed consent in the newborn screening process. In order to provide maximum respect for persons who participate in newborn screening, including both infants and their parents, professionals who have contact with infants and parents in the newborn screening process should explain the possibility of future use of samples beyond the immediate purposes of newborn screening. Parents may agree to coded or to fully anonymous use of their children's samples in future research. However, the investigator should include in the information imparted to parents the possibility that newly discovered information might be of consequence to their children or to themselves. Parents who elect coded use of their children's samples might choose to receive such information at some future time, while parents who opt for fully anonymous use of samples should understand that such use precludes the possibility of conveying new information to themselves or their children. Finally, some professionals are skeptical about the capacity of parents to give blanket consent for future use of stored samples. However, if information about genetics and the ramifications of future studies is presented to parents clearly and carefully, then they should be prepared to make a rational and informed decision about future use of the samples that they or their children have supplied or donated.

Obligations to Source Persons

The fact that clinicians and researchers in human and medical genetics have hesitated about using archived tissue samples indicates an intuitive awareness of respect for persons who are the sources of surplus or archived samples. This intuition indicates, on the one hand, that source persons, or the parents of infant sources, should have at least some role in deciding about future use of samples. However, researchers who are primarily oriented toward developing new knowledge, in the "academic" sense, argue that anonymous use of old samples is not only justified, but is also separate and apart from any obligation to the source person.

Ideally, the professional who hopes to use collections of archived samples would be able to contact all source persons, or their families, and would be able to obtain current informed consent with little or no trouble. However, in a highly mobile society, with unstable family structure, such a scenario is unrealistic, and the logistics of recontacting parents of former newborn populations looms as a massive and even prohibitive obstacle. The genetics professional is therefore charged with finding a solution that will be practical for research as well as respectful of individual rights.

With respect to collections that were assembled in the past, protocols for newborn screening were narrowly directed toward immediate identification of affected infants. These protocols were developed before the advent of molecular genetic techniques that have greatly increased the investigative value of archived samples. In any attempt to balance the immense logistical problems of obtaining new consent for using old samples against the immense knowledge that may be derived from contemporary research efforts, research geneticists may logically argue that the most benefit to mankind will be realized by permitting anonymous use of existing collections of samples. Conscientious researchers and policy consultants may strive for the ideal of recontacting parents while simultaneously developing reasonable requirements for genetics investigators.

Protocol for Informed Consent

Professionals in genetics have indicated a good faith awareness of the ethical and legal implications of using archived tissue samples from newborn screening programs, and the professional community is now in the process of instituting new protocols that will provide for obtaining parental consent, in the present, for use of samples in the future. Parents who are now participating in newborn screening programs should be approached with information about the immediate purposes of screening and about possible future use of the tissue samples. Consent for both screening and future use of samples should be elicited in two steps, and parents should be confronted with a single, dichotomous choice for each distinct issue. Each opportunity for choice should be presented in clear, concise language, with a simple, clear choice at each step.

The preliminary step in obtaining requisite consent for use of samples in research is obtaining consent for including the individual in a genetic screening program. Thereafter, consent for using samples in future research would include a description of the current or proposed research project, followed by an explanation of the options available for the participants (Fig. 1, 2, and 3). The options should include information about the right to withdraw without prejudice and the right to alter an earlier decision if this

is still feasible. The third element is a direct question about willingness to participate. The second step (Fig. 1) is an offer to convey any new information to the participant, if the participant elects to receive that information. The language in Question 4A describes only the existence of new information, and notification of its existence, and not the content or substance of the information. The next question, 4B, follows directly on the preceding one: if the participant chooses to be informed, the next choice is how the information should be conveyed. Once the issue of feed-back is addressed, the possibility of using left-over tissue samples may be presented [Questions 5A and 5B]. Question 5A solicits consent for use of archived samples in future studies. Finally, Question 5B acknowledges conditions of consent - the consequences of using samples with or without identifiers or codes, and the issue of feed-back when new information is available. If the participant has indicated a willingness for the leftover sample to be used in future studies, then he or she must decide about having access to any new information. The participant should have a clear understanding that a choice to remove all identifiers is both a safeguard of personal privacy and a waiver of the opportunity to receive any new information that may be generated in the future.

Summary and Conclusions

The new dilemmas of informed consent in newborn screening are not difficult problems to overcome. Perhaps the most reasonable solutions to these dilemmas will rest on devising one set of guidelines for the use of old collections of samples that are already housed in archives, and a second set of guidelines that will govern informed consent and the use of collections that are assembled now and in the future.

Existing collections of samples may be reasonably used for research purposes under two sets of circumstances. (1) If at all possible, source persons, or their parents, should be (re)contacted for specific, current consent. This approach affords maximum respect for the personal autonomy of source persons, although practical logistics may be formidable, or even insurmountable. (2) If specific, current consent cannot be obtained from source persons, their archived samples may be used for research provided that they are uncoded and are completely anonymous. The first of these approaches would provide maximum flexibility for the source person to learn about new genetic information, while the second approach would preclude any further contact with the source person -a situation that could abrogate at least some of the source person's further right to exercise his or her own autonomy.

Protocols for collecting samples now and in the future should include provisions for obtaining parental consent for newborn screening. This consent protocol should also include information about the possible future use of samples for novel genetic studies. Choices that are presented to parents should be clearly worded and clearly dichotomous. With some attention to these ideas, genetics professionals will create interactions that, on the one hand, are respectful of individual rights and personal autonomy, and, on the other hand, are compatible with the interests of the medical and scientific research community.

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Figure 1

Future Use of Archived Samples in Genetics Research: Protocol for Informed Consent

General Information:

1. Description of the research project

2. Options for the participant, including the right to withdraw without prejudice

3. Do you wish to participate?

   Yes _____ No _____

4A. We may develop new information about your genotype or the genotype of your child. If we do, would you like to be notified that the new information is available?

   Yes _____ No _____

4B. Sometimes new information can have serious implications... If you decide to learn the new information, how would you prefer to receive the information?

   Phone _____ Letter _____ Clinic visit _____

   Decide later _____

5A. We may have some of your tissue, or blood, left over after our current study is completed. Would you consent to the use of this tissue in future studies...

   by us? Yes _____ No _____

   by other researchers? Yes _____ No _____

5B. If your samples are used with personal identifiers or with coded identifiers, it will be possible to contact you when new information is available.

   If your samples are used with no identifiers or codes, it will not be possible to contact you when new information is available.

   Would you prefer to have your samples used with identifiers or codes _____, or without identifiers or codes _____?

Legal Implications of Genetic Service Guidelines*

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By whatever name they go -- practice parameters, service guidelines, clinical indicators -- these strategies to assist physicians in patient management have become hot topics among physicians and their professional organizations, among managed care organizations and health care payors and, of course, among the lawyers that serve them. Their numbers are somewhat staggering: last year, the AMA/Specialty Society Practice Parameters Partnership estimated that almost 1600 guidelines have been promulgated by approximately 70 physician organizations and other groups; many more are currently under development.[1] The Institute of Medicine found that guidelines "have been linked in recent years to almost every major problem and proposed solution on the American health policy agenda . . . . [including] costs, quality, access, patient empowerment, professional autonomy, medical liability, rationing, competition, benefit design, utilization variation, [and] bureaucratic micromanipulation of health care . . . ."[2]

This recent ground swell of interest in guidelines has been accompanied by questions regarding their legal implications. Health care providers wonder how the implementation of guidelines will affect their malpractice liability risks. Medical societies are concerned about their liability exposure in connection with the development and publication of guidelines. In addition, questions have been raised about the potential liability of managed care organizations and payers who may rely on guidelines in making utilization review and payment decisions.[3]

This afternoon, I would like to spend a little time discussing the first issue -- that is, the general effect of guidelines on the malpractice liability risks of health care providers -- and then focus on the potential liability of organizations such as the Council of Regional Networks for Genetic Services (CORN), the American College of Medical Genetics (ACMG), and the National Society of Genetic Counselors (NSGC) which currently are involved in the development of genetic service guidelines. I am not going to address the potential liability of payers -- they can take care of themselves.

Malpractice Liability

The greatest fear of health care providers with respect to guidelines is that if they deviate from a guideline, even for legitimate medical reasons, and a bad outcome results, they will be automatically liable for malpractice. Their greatest hope is that they will be automatically cleared of any liability if they comply with the guideline. Neither scenario is likely to be true. Although only a few cases have arisen in which guidelines have been offered as evidence, these cases indicate that courts are likely to admit the guidelines, but unlikely to apply them as conclusive standards of care.[4] Rather, guidelines, if relevant and reliable, generally will be viewed as "some evidence" of the standard, similar to journal articles, learned treatises, and medical textbooks, the contents of which are persuasive but generally not dispositive.[5]

There are two exceptions to the general rule that guidelines will not be admitted as conclusive evidence of the applicable standard of care. The first is the rare circumstance in which a guideline has in fact been developed and widely accepted as a professional standard, i.e., as a minimal requirement applicable in all cases. In such circumstance, the guideline may be admissible as an "industry" standard, and deviation from the guideline may indeed constitute a per se indication of negligence.[6] The second exception is where legislative action determines that compliance with a guideline is conclusive evidence of due care. An example of such action is the Maine Medical Liability Demonstration Project.[7] Pursuant to this statute, each of several medical specialty advisory committees is to develop (1) practice parameters to "define appropriate clinical indications and methods of treatment," and (2) risk management protocols "designed to avoid malpractice claims and increase the defensibility of the malpractice claims that are pursued."[8]

Physicians must give notice of their intent to participate in the Project.[9] The Project includes several incentives for participating physicians: (1) if the physician is sued for malpractice, he or she can introduce the relevant practice parameter or risk management protocol as an affirmative defense along with evidence of his or her compliance therewith; (2) in order to prove negligence, the plaintiff has the burden of proving noncompliance; and (3) a plaintiff may not introduce a practice parameter or risk management protocol developed by the Project as evidence of negligence.[10]

In general, however, guidelines will not be determinative of malpractice liability. Nevertheless, they should have a positive effect on the fairness and predictability of malpractice litigation. They should, at a minimum, reduce one of the most disturbing problems in litigation today: the battle of the so-called experts. "The hired gun will be challenged to defend his [or her] opinion against that of preeminent practitioners in the field."[11]

Once a guideline has been admitted, the other side will be allowed to introduce competent experts and authorities that disagree with the guideline. As guidelines proliferate, there will likely be cases in which a jury is asked to choose between conflicting guidelines.[12] In this connection, it is important to emphasize the value of consensus. Conflicting guidelines will confuse health care providers and will diminish the evidentiary value of a guideline in court. Moreover, where significant controversy exists regarding a particular practice, it is probably not an appropriate subject for a guideline. The persuasiveness of any given guideline will depend upon a number of factors including its source and purposes, the method by which it was developed, the strength of the consensus by which it has been accepted, and its applicability to the specific case.[13]

Well-developed guidelines will provide judges and juries with "access to the informed thinking of the profession, and reduce dependence upon experts whose personal opinions may differ from the professional norm."[14] This will, hopefully, produce a greater percentage of "correct" litigation results, i.e., verdicts for defendants where no negligence is present and verdicts for plaintiffs where negligence has occurred.[15] In addition, the existence of a well-developed and generally accepted guideline may deter meritless malpractice claims and promote settlement of meritorious cases.[16]

Liability of Standard Setting Organizations

Physician associations and other medical societies that engage in the development of guidelines may expose themselves to liabilities which they otherwise would not have including both antitrust liability and tort liability for negligent standard setting.

A. Antitrust Liability

The antitrust laws prohibit concerted activity that restrains trade or harms competition.[17] If a medical society develops guidelines, some providers, particularly those who practice in a manner inconsistent with the guidelines, may believe that the guidelines injure their ability to compete; i.e., to attract patients and obtain payment for their services. In such circumstances, they might decide to bring an antitrust action against the organization that developed the guidelines.[18]

These lawsuits are unlikely to succeed unless the procedures by which the guidelines were developed have been significantly tainted by anticompetitive motivation or unfair procedures.[19] Nevertheless, it is worth spending a little time trying to understand the nature of an antitrust claim and the safeguards that should be observed to comply with federal and state antitrust laws.

To succeed in an antitrust action against a medical society for the development of service guidelines, the plaintiff health care provider would have to prove that (1) the organization had engaged in concerted action and (2) that the concerted action had unreasonably harmed competition in the market for his or her services. "Concerted action" generally will be found whenever two or more entities agree on a certain course of conduct. Thus, an agreement between two or more separate medical societies is clearly concerted action. However, the policies and practices of even a single medical society generally will be treated as concerted action on the theory that the organization constitutes a continuing agreement among its members who otherwise compete with one another in their medical practices[20], a so-called "walking conspiracy." Thus, the development of a genetic service guideline by an organization of geneticists ordinarily would satisfy the concerted action requirement for an antitrust case.

The principal question then becomes whether the guideline imposes an unreasonable restraint of trade. The restraint is "unreasonable" if its net effect is to suppress competition. “Whether the conduct results in other social benefits -- for example, improving the quality of medical care or protecting the public from charlatans -- is relevant only to the extent that these benefits themselves promote competition.”[21] The establishment of guidelines may, in fact, have a significant procompetitive effect. Guidelines can provide useful information to providers, patients, and payers, and may assist them in making rational treatment and utilization decisions.[22]

In analyzing the pro- and anti-competitive effects of guidelines, one of the key questions will be whether the medical society enforces the guidelines through some type of coercive action; if not, the guidelines should not violate the antitrust laws.[23] For example, in the 1989 case of Schachar v. American Academy of Ophthalmology, the Academy had issued a press release stating that the procedure of radial keratotomy was experimental. It urged patients, ophthalmologists, and hospitals to consider the procedure with caution until additional research had been done. A group of ophthalmologists who

performed radial keratotomy sued the Academy. The court held that when an association "provides information . . . but does not constrain others to follow its recommendations, it does not violate the antitrust laws."[24]

The court's opinion is particularly instructive in its emphasis on what the Academy had not done:

> "It did not require its members to desist from performing the operation or associating with those who do. It did not expel or discipline or even scowl at members who performed radial keratotomy. It did not induce hospitals to withhold permission to perform the procedure, or insurers to withhold payment; it has no authority over hospitals, insurers, state medical societies or licensing boards, and other persons who might be able to govern the performance of surgery."[25]

In fact, the opinion in Schachar goes on to suggest that, absent some enforcement mechanism, the development and dissemination of guidelines by a medical society will not be found to violate the antitrust laws even if those guidelines are "false or misleading or incomplete or just plain mistaken."[26]

If, however, a medical society does appear to use guidelines as a mechanism for policing and directing professional practices, the antitrust analysis will focus on the reasonableness of the guidelines; specifically on their purpose, their scientific and clinical validity, and the propriety of the procedures by which they were developed.[27] In general, if the medical society develops guidelines in good faith, i.e., without anticompetitive motivation, for a legitimate purpose, and through impartial procedures which consider all relevant scientific and clinical information and opinions, the guidelines should actually enhance rather than suppress competition and there should be no antitrust violation.[28]

Liability for Negligent Standard Setting

A medical society that develops service guidelines potentially exposes itself to liability for negligent standard setting. If a patient is injured as a result of services rendered, or not rendered, by a health care provider who relied on the society's guidelines, the patient is likely to sue the provider and may, in addition, sue the medical society. One theory of liability would be that the patient would not have been injured had the medical society not developed and disseminated information that was incorrect or otherwise not in keeping with the established standard of care. Essentially, the allegation would be that the medical society was negligent in its development of the service guidelines, and the patient's health care provider was negligent in relying on the guidelines. So can the medical society be held liable?

If you had asked me this question last May, my answer would have been, and in fact was "not likely."[29] In the analogous context of product standard setting, although several cases had recognized the possibility of a valid claim for negligent standard setting, there were no cases in which a trade association actually had been held liable for negligently developing product safety standards.[30] There are a number of reasons for this.

First, as many of you know, the initial element that a plaintiff must prove in a negligence case is the element of "duty," i.e., that the defendant owed a duty of care to the plaintiff. Claims against trade associations for negligent standard setting generally fail because, ordinarily, the association owes no duty to the general public, including consumers who use products manufactured by association members.[31]

Thus, for example, in the 1987 case of Meyers v. Donnatacci, a New Jersey appellate court held that a nonprofit swimming pool trade association that promulgated suggested minimum safety standards for the design and construction of swimming pools did not owe a duty to an injured pool owner to support a finding of negligence.[32] The court reasoned that the association did not control the conduct of its members and "had absolutely no power to force a member to comply with its promulgated standards."[33] Further, the court recognized that imposing such a broad duty would undercut the "laudable purposes" served by nonprofit associations.

Similarly, a medical society should owe no duty of care to patients who receive services furnished by the society's members. Medical societies do not dictate the care provided to patients by their members. Even the most authoritative body of guidelines would not displace the health care provider's responsibility to make treatment decisions according to his or her best medical judgment and in light of the specific clinical circumstances of his or her patient.[34] Moreover, public policy considerations do not warrant treating medical societies as insurers of patients' medical outcomes; providers and hospitals generally have sufficient liability coverage to ensure appropriate compensation.[35]

In addition to the absence of a duty, up until last May, I also would have said that a plaintiff would have a difficult time establishing that a medical society's conduct in developing guidelines was the proximate cause of his or her injuries, since the immediate cause is presumably the independent judgment of the health care provider.[36] The patient would have to show, at a minimum, that the health care provider relied on the guidelines and that, if not for the guidelines, the provider would have acted in a manner that avoided injury to the patient.

In short, up until last May I would have said that the law of negligence does not support the imposition of liability upon medical societies for negligent standard setting. Then, on June 5, 1995, the Appellate Division of the Superior Court of New Jersey decided the case of Snyder v. American Association of Blood Banks.[37]

In Snyder, the appellate court affirmed a jury's verdict that the American Association of Blood Banks (AABB), a not for profit association whose members include most of the country's voluntary blood banks, was liable to a surgery patient who had contracted HIV from a blood transfusion in August of 1984. The court held that the evidence presented at trial supported the jury's finding that the AABB had acted negligently in failing to recommend that its member blood banks perform surrogate testing to screen out high risk blood donors. The jury had found that the AABB's failure in 1984 to recommend surrogate testing, and its affirmative recommendation to member blood banks not to test, was, in light of what was known about HIV transmission prior to the plaintiff's surgery in 1984, clearly imprudent, unreasonable, and negligent.[38]

The court rejected the AABB's argument that it owed no duty of care to the plaintiff. The court noted that "[t]he AABB's raison d'etre is to assure that the recipients of blood supplied by its institutional members receive as safe a product as is reasonably practical."[39] Further, the court found that the "unique and dominant role of AABB in blood-banking and the extent of its control over its institutional members create the requisite relationship between it and the ultimate recipient whose safety is its avowed paramount concern."[40]

The court also found sufficient evidence of causation. The court framed the question as "whether the risk that plaintiff would be infected by HIV in August 1984 was enhanced because [the blood bank] did not perform [surrogate testing] for AIDS and whether [the blood bank's] failure to do so was directly attributable to AABB's . . . .nonrecommendation to its institutional members."[41] The court found that the evidence supported the jury's affirmative answer to this question. Snyder is currently on appeal to the New Jersey Supreme Court. Even if it is upheld, it will be binding law only in New Jersey. However, to the extent that the force of its reasoning persuades courts in other states, it may be followed.

Snyder is, on its facts, somewhat distinguishable from what we would expect in a "typical" standard setting case. For one thing, both the jury and the appellate court clearly found the AABB's conduct to be egregious, "resulting in unnecessary contamination of the blood supply."[42] In addition, the AABB has the authority to require its members to comply with its standards, although the policy on surrogate testing apparently was not a required standard.

The bottom line, however, is that under the Snyder rationale, a genetics society that establishes standards for the provision of medical genetic services could face liability to a patient who is injured as a result of a health care provider's reliance on those standards. Suppose, for example, that the society failed to modify its service guidelines to reflect current studies showing that a certain carrier test was valid and should be performed in particular clinical circumstances or on the general population.[43] Suppose, moreover, that a geneticist or genetic counselor or obstetrician, relying on the guidelines, did not inform his or her patient of the availability of the test. Finally, suppose that the test would have revealed that a patient and her spouse were both carriers for a serious genetic disorder. If the couple goes on to have an affected child, they might have a cause of action against the physician for wrongful birth and against the genetics society for negligent standard setting.

Even in these circumstances, however, it would be necessary for the plaintiff to show (1) that the society's actions in not recommending the test were unreasonable and, thus, negligent, (2) that, if not for the society's guidelines, the health care provider would in fact have informed the patient about the test, and (3) that, had the patient been informed of the availability of the test, she would have had it performed and would not have given birth to an affected child.

There are a number of precautions that a genetics society may take to minimize the risk of liability for negligent standard setting. First, guidelines should be developed and maintained according to fair

procedures designed to assure objectivity and scientific validity. In addition, they should be reviewed and updated regularly, and reconsidered if important new information calls into question the validity of the guideline. Finally, they should be accompanied by a disclaimer that advises health care providers that, in determining the propriety of any specific procedure or test, the provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient.

In summary, there is some potential liability for professional associations and medical societies engaged in the development of genetic service guidelines. I would like to conclude by giving you some suggestions for guideline development that take into account concerns regarding (1) quality care for patients, (2) malpractice liability of providers, and (3) antitrust and tort liability of the medical society (Table 1).

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3. American Medical Association, Legal Implications of Practice Parameters 1 (1990) ("Practice Parameters"). See, e.g., Wickline v. California, 239 Cal. Rptr. 810 (Cal. App. 1986) (suggesting that a physician's adherence to utilization criteria designed primarily to cut costs provides little protection against a claim of negligence).

4. West, The Legal Implications of Medical Practice Guidelines, 27 J. Health & Hosp. Law 97, 100-101 (1994) ("Medical Practice Guidelines").

5. Id. at 101.

6. See, e.g., Roach v. Springfield Clinic, 585 N.E.2d 1070, 1079 (Ill. App. 1991) ("Relevant industry standards are usually admissible to show a standard of care."), rev'd on other grounds, 623 N.E.2d 246 (Ill. 1993).

7. ME. Rev. Stat. tit. 24, §§2971 - 79. (1994).

8. Id. at §2973.

9. Id. at §2976.

10. Id. at §2975.

11. See Medical Practice Guidelines, supra note 4, at 99.

12. Bierig, Raskin & Hirshfeld, Malpractice Considerations for Physicians 20 in Practice Parameters, supra note 3.

13. Id. at 20-22.

14. Id. at 23.

15. Id.

16. Id.

17. 15 U.S.C. §§1, 45.

18. Bierig, Raskin & Ile, Antitrust Considerations for Medical Societies 27 in Practice Parameters, supra note 3.

19. Id.

20. Id. at 28.

21. Id.

22. Id. at 32.

23. Id. See also Schachar v. American Academy of Ophthalmology, 870 F.2d 397, 397 (7th Cir. 1989) ("There can be no restraint of trade without a restraint.").

24. Schachar, 870 F.2d at 399 ("An organization's towering reputation does not reduce its freedom to speak out.").

25. Id. at 398.

26. Id. at 400 ("the remedy is not antitrust litigation but more speech -- the marketplace of ideas.").

27. Bierig, supra note 15, at 36-38.

28. Id.

29. See Bierig, Raskin, Fleisher & Hirshfeld, Tort Liability Considerations for Medical Societies 43-54 in Practice Parameters, supra note 3.

30. Id. at 44.

31. Id. at 45.

32. Meyers v. Donnatacci, 531 A.2d 398 (N.J. Super. 1987).

33. Id. at 403.

34. Bierig et al., supra note 29, at 45.

35. Id.

36. Id. at 45-46.

37. Snyder v. American Association of Blood Banks, 659 A.2d 482 (N.J. Super. 1995).

38. Id. at 490.

39. Id. at 492.

40. Id.

41. Id. at 492-93.

42. Id. at 490.

43. Bierig et al., supra note 29, at 48-49.

44. See Bierig et al., supra note 12 at 25-26, supra note 18 at 42, and supra note 29 at 53-54.

Table 1

Development of Medical Service Guidelines:
Suggestions for Minimizing Liability Risks[44]*

PROCESS: Develop guidelines in accordance with defined procedures to assure scientific validity and objectivity

1. Based on thorough scientific and medical review
2. Avoid political and economic considerations (or indicate their consideration)
3. Utilize fair and objective procedures and avoid potential conflicts of interest
4. Provide for outside review and comment
5. Attempt to achieve consensus
6. Review and update regularly and modify as necessary
7. Do not police compliance or lobby inappropriately for adoption

CONTENT: Guidelines should reflect the full range of acceptable medical practices

1. Indicate level of professional consensus
2. Neither too stringent nor too permissive
3. Avoid extravagant claims regarding efficacy
4. State what guidelines do not address

DISCLAIMER: Clarify limitations and applicability of guidelines

1. Guidelines are voluntary and educational
2. Adherence to guidelines does not assure successful medical outcome
3. Acceptable medical opinions and practices may vary and other sources of medical information may be relevant
4. Guidelines are not intended to displace health care provider's best medical judgement based on clinical circumstances of individual patient
5. Providers should document reasons for significant deviation from guidelines
6. Guidelines are developed for patient care purposes -- not for reimbursement, credentialing, or utilization review decisions

Legal and Ethical Issues: Consumer Perspective

S. Wagoner. Washington, D.C.

Introduction

I'm going to talk today about my views as a dad and I'm also here as a representative of the Alliance of Genetic Support Groups. I am proud to be here as a representative of the families we serve and, hopefully, I'll be able to provide a little food for thought for when you see those families for the very first time, or for the thirtieth time, and give you an idea of some of the things that may be running through their minds and through their hearts.

Those of us who come in on the patient end of genetic services wear many hats. I wear several different hats in my daily life: an Air Force hat in my profession, the "hat" of being a dad, and there are a lot of other different areas I'm involved in, of which I bring a lot of baggage along with me when I do them. Consumers, your patients, their families - they're all different. They are increasingly informed, particularly with the Information Superhighway and the accessibility of data. They're also increasingly misinformed, so it's very important that we all recognize from both perspectives that we may have good information and we may have bad information, but we all have varying perspectives on the issues.

Today I bring many perspectives. I look at issues from a dad's perspective and I'm also the brother of a woman with narcolepsy. I don't have much legal background but I still tend to advocate just a bit and I also see myself as most of us should - as a future patient. We are all temporarily healthy. Someday we will all be on the receiving end of healthcare. I look at things based on my experience and my values that I was taught while growing up in South Central Kansas, as well as those values I've learned as I've moved around. I tend to go by what my heart tells me -- my emotions. I think you'll find that most consumers share these same perspectives. Again, personally I have a 4 year old son who happens to have an extra X chromosome. You would never know it by just looking at him. When we were first diagnosed prenatally, we were counseled that abortion was an option. The level of information we were given at that point was very important to the decision process, regardless of what our views were on that issue.

Some of the things I'd like to talk about in particular are relationships, both with the institutions (medical institutions, insurance institutions) and our personal relationship with our families. We also have a lot of concerns. Many of these concerns are held in privacy while the rest may relate to some of the issues that have been discussed in this conference. What is the consumer role in healthcare? What do we need to do to get the appropriate care, information, and the appropriate future outlook for those family members that are affected by insurance concerns? As you all know, medical care and health requirements can be financially devastating on some families.

I'd like to talk about the institutional relationship with the medical community. One of the most important things to remember when we all enter this arena is that we're all coming into it anew. Many families are second-generation diagnosis but at some point, we enter the process for the first time and

it's very critical that a responsible diagnosis occurs at that time. How do we get the information? As many speakers have already said, we want to send a letter, make a telephone call, or a clinical visit. How is that information relayed back to us? The healthcare system, sensitive to our needs, sets up our perspectives and our outlook as to (1) what are our expectations? and (2) what is our view of just how much this system is either helping us or imposing itself upon us.

Informed Consent

I can't add much to what was already said, so I won't try. But, again, informed consent is an issue of concern. Families expect to know what's going to be done with our bodily tissues, what those tissues are going to be used for, and to have the opportunity to make appropriate choices.

You will find a wide array of consumer sensitivities to the institutional labels of our children. I have a hard time looking at my 4-year old son as defective or diseased. We all recognize that there are appropriate uses of those terms within the medical community, but there are also great sensitivities on the families in having our children or ourselves labeled.

Another issue that we need to look at is family rights. As more and more tests are coming out, more and more diagnosis are possible. We become more sensitive to telling our family. Do I tell grandma we have this trait or do I tell my children they have a possibility of passing something on to the next generation? How do I tell my son that he can't have children and when should I tell him? The more information we have, the more concerns we develop on what exactly are our families rights. Who do we tell that they're potentially at risk? Who do we tell that may not necessarily be affected, but who might have an interest in the welfare of that family member. Who has a right to know and a right not to know? There are many, many ethical dilemmas that the families face. And, again, there is no "cut-and-dried" solution to any of this, but these are perspectives that you, the medical community, will be and are confronted with. We recognize this happens on a day-to-day basis and we need to work together.

The General Medical Community

When the test results come in, what's the legitimate use of those tissue samples? How are the insurance companies going to handle things? Again, financially devastating results can occur through cancellation of insurance coverage, denial of healthcare, and loss of jobs. You'll find families that are torn as to even telling anybody about it, whether that be the family member who is affected or the insurance company. So, do you worry about insurability and being fully disclosive to an insurance company or do you conceal the problem and all the legal implications associated with concealing preexisting conditions? And is it just a trait or is it a preexisting condition? Again, the more diagnosis we get, the more genes that are identified as possibly leading to something in later life. Then we have the dilemma with the insurance company. Where do we cross the line between just having blue eyes and having some terrible outcome when we're 40, 50, or 60 years old and, therefore, lose the coverage.

Employment

There's been some progress on the employment side, in that the EEOC guidelines have addressed the genetics issue but there are still day-to-day concerns out there on the part of families.

Schools

How are the children labeled in the schools? Will there be terms that we all grew up with such as retarded, slow, special? What funding issues go along with those labels? Do schools get more money because they have "X" number of children in a special needs class? How are these decisions made in the schools? These are just some of the concerns that the family will be carrying with them when they interact with the medical community and the school systems.

Conclusion

Families have very basic needs. Families have different perspectives. They can be an experienced advocate or they can be a novice. They can be a team mate with their healthcare providers or they can be a victim of the system. They simply want to care for their affected family members with limited collateral damage and have the problem taken care of with as few issues to deal with as possible.

Figure 1

Figure 2

Uncharted Territory of Familiar Shoals?

★ **Consumer Perspectives Driven By:**

- Role
  - > Father, Spouse, Brother, Layman, Advocate, Future Patient
- Outlook
  - > Experience, Knowledge, Values, Emotions

★ **4 yr old son, "Xtra X"; 50 yr old sister, Narcolepsy**

Figure 3

Issues of Concern

★ **Relationships**
- Institutional
- Personal

★ **Access**
- Health Care
- Insurance
- Education
- Employment

Figure 4

Institutional Relationships

★ **Medical Community**

- Responsible Diagnosis
  > Appropriate Information/Sensitivity
- Informed Consent
- Labeling: "defect", "disorder"
- Privacy

★ **Others**

- Insurers
- Employers
- Schools

Figure 5

Privacy Concerns

★ Family Rights? (potentially at risk/merely interested)

- Right to know/right not to know?

★ General Medical Community? (legitimate research?)

★ Insurance companies?

- Insurability vs. concealment
- Genetic trait vs. "pre-existing condition"

★ Employers?

- Employment Discrimination
  > EEOC Guidelines

★ Schools

- Labeling

Figure 6

“Life, Liberty, etc.”

★ Professional Care ★ Respect for Privacy

★ Financial Stability

Assessing the Performance of Screening and Diagnostic Tests

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Introduction

The fundamental principles that guide assessment of screening and diagnostic tests are the same, irrespective of the area of medical practice being served.[1] The first step involves determining whether the medical condition which the test aims to detect is of sufficient importance to warrant attention. If the medical condition is not serious or occurs only as a rare event, then the test is likely to be of limited value. Some useful purpose needs to be gained by identifying the medical condition, such as reducing morbidity and mortality or avoiding clinical manifestations altogether. When the test is used for screening purposes, some definitive follow through needs to be available for individuals with positive screening results, in the form of a diagnostic test and/or a preventive treatment. The detection rate (sensitivity) for any test is defined in terms of the proportion of individuals with the medical condition who can be identified by the test. While this sounds simplistic, all too often the medical condition and, by extension, the quality of test performance are incorrectly described. Cholesterol and blood pressure measurements are prime examples. The false positive rate (1-specificity) describes the proportion of individuals without the medical condition whose test results will be positive. The clinical significance of the false positive rate depends upon: 1) whether the test is for screening or diagnostic purposes; 2) the frequency of the medical condition in the population being served; and 3) the cost and safety of follow-up testing or treatment. A helpful additional calculation involves determining the odds that an individual with a positive test result actually suffers from the medical disorder. This calculation can be made by knowing the detection rate and false positive rate of the test, and the prevalence of the medical condition in the population being tested. Lastly, the costs of testing (both economic and medical) need to be determined, as a final step in judging efficacy. A checklist for performance assessment, published by Wald and Cuckle, is reprinted here to further guide those carrying out such evaluations[1] (Table 1).

An Example of Performance Assessment

As an example, the efficacy of various prenatal screening protocols for detecting fetal Down syndrome can be readily compared, using the guidelines discussed in the preceding paragraph. Table 2 shows several screening protocols that either are used now or have been used in the past. Two proposed screening protocols are also shown. Estimated costs for the various tests and procedures are as follows: serum alpha-fetoprotein interpretation, $5.00 (the test is already being performed for open neural tube defect screening); serum unconjugated estriol and human chorionic gonadotropin measurement and interpretation, $40.00; amniocentesis, ultrasound and chromosomes, $1,000.00. Amniocentesis-related fetal loss is estimated to occur in one per 200 pregnancies having the procedure. The calculations all assume total participation. The age distribution of pregnant women is taken from 1993 census figures (10.5 percent of pregnant women are >35 years old). In this table, actual numbers of pregnancies are tallied, rather than just percentages, to provide a more tangible source for comparing the various screening strategies. The line that lists the number of amniocenteses is equivalent to the false positive rate, and the Down syndrome cases detected expresses the detection rate. Amniocenteses performed

per case detected is equivalent to the odds of being affected, given a positive screening result. The Down syndrome cases detected are based on birth prevalence, rather than second trimester prevalence.

The efficacy of the first prenatal screening test for Down syndrome (asking a woman her age) is shown in the first column. In the population of one million pregnancies, 105,000 would have amniocentesis and 548 cases of Down syndrome would be detected. For every Down syndrome case identified, 190 amniocenteses would be necessary, and, overall, 523 fetal losses would occur. The cost per case detected would be $190,000.

The second column shows the impact of adding maternal serum AFP screening in younger women to the existing maternal age-based protocol. Amniocenteses, Down syndrome cases detected, fetal losses and total costs all become greater. The efficiency of screening, however, remains unchanged, as measured by the amniocenteses required to detect each Down syndrome case and by the cost per case detected.

In the third column, multiple marker screening replaces maternal serum AFP in the younger women. Again, the total number of amniocenteses rises, but the number of amniocenteses required to detect each Down syndrome case is lower, for the first time. The cost per case detected, however, remains unchanged.

The fourth column simulates a protocol that has developed at a number of prenatal care sites in the United States, in which a proportion of women >35 years old opt for multiple marker screening, rather than choosing amniocentesis, directly.[2] This mix-and-match approach yields further improvement in the ratio of amniocenteses performed to Down syndrome cases detected. It also is associated, for the first time, with a lower cost per case detected.

Two other screening protocols have been proposed in recent years but are not in general use. These are shown in the two right-hand columns. The first abandons maternal age as a screening test and applies multiple marker screening to pregnant women of all ages.[3] This protocol is, by far, the most effective when judged by both the ratio of amniocenteses to Down syndrome cases detected and the cost per case detected. In spite of this, it is unlikely that the maternal age screening test will be withdrawn, because it is so familiar and well established.

The second proposed screening protocol calls for lowering the maternal age cut-off to 30 years for amniocentesis.[4] Women younger than 30 years would be offered multiple marker screening. While more total cases of Down syndrome are detected by this approach than by any other, it requires that 35 percent of all pregnant women undergo amniocentesis. The inefficiency of this protocol is reflected in the very high number of amniocenteses necessary to detect each Down syndrome case, the very high cost per case detected, and the high number of amniocentesis-related fetal losses.

Conclusion

It is important for physicians and others involved directly in patient care to develop analytic skills such as are described here, if they are to maintain at least a portion of the decision-making initiative in allocating health resources. Dollar resources for health care are likely to continue tightening for the foreseeable future, making decisions about how to invest those dollars more critical. Traditionally, physicians have found such decision-making awkward and unpleasant. By using a consistent framework such as described here, physicians and other health care providers can develop a solid foundation, both in relation to cost and health impact, upon which to build an advocacy position for their patients.

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Table 1

Checklist for the Assessment of Screening or Diagnostic Tests.
The Test 1. Is the test a screening or a diagnostic test? 2. Is it one of several tests or enquiries? 3. If so, are the tests carried out in series (e.g. only those whose first result is positive have a second test and so on) or in parallel (everyone has all tests)?
The Disorder 4. What is the disorder that the test is designed to detect? 5. Can the disorder be defined without reference to the test? 6. What is its natural history? 7. Is the natural history of those with positive tests similar to the natural history of those with negative tests?
Prevalence of the Disorder 8. What is the prevalence of the disorder in the population to be tested? 9. What method was used to determine prevalence?
Therapeutic Intervention 10. If it is a screening test, what diagnostic test will follow and what therapeutic intervention if that test is also positive? 11. If it is a diagnostic test, what therapeutic intervention will follow a positive result? 12. What is the justification for this therapy?
Test Results 13. Is the test or enquiry quantitative or qualitative? 14. If it is quantitative (e.g. maternal serum AFP level), what is the distribution of screening test results in affected and unaffected subjects? 15. If it is qualitative (e.g. cervical smear test), what are the possible definitions of a positive result?
Test Performance 16. What is the detection rate? 17. Has this been determined from a complete series of affected individuals in which any with negative results were not overlooked? 18. What is the false-positive rate? 19. What are the odds of being affected given a positive result? How will this vary according to the prevalence of the disorder? 20. For quantitative results, what is the effect of changing the cut-off level on the detection rate, false-positive rate, and the odds of being affected given a positive result? 21. Can a flow diagram be constructed with 100,000 individuals and ending with the final outcome, segregating affected from unaffected at the outset?
Cost and Benefit Analysis 22. What are the medical costs and benefits? 23. What are the financial costs and benefits? 24. Can a balance sheet be drawn up for each, including any suffering that will be alleviated through the application of the whole testing process and at what cost and medical intervention?
Evaluation of the Tests 25. Is the test better than other tests when comparison is made of their respective detection rates and false-positive rates? 26. Does it offer an advantage over other tests to such an extent that it should replace an existing test or be added to it and used in combination?
Practical Problem 27. What are the practical problems in implementing the test as a screening or diagnostic procedure? 28. Are special facilities required? 29. If so, what is their availability or ease of installation?

Table 2

Screening 1,000,000 Pregnancies for Down Syndrome (DS): Comparison of Protocols						
	Screening Protocols Currently or Historically Used				Screening Protocols Proposed	
	Age >35	Age ≥35 & MSAFP <35	Age ≥35 & AEH <35	Age ≥35 Mix AEH <35	AEH All Ages	Age ≥30 AEH <30
Amnios required (% of population)	105,000 (10.5)	120,000 (12.1)	140,000 (13.5)	112,500 (11.3)	57,500 (5.8)	352,500 (35.2)
DS Detected	548	648	960	932	873	1,100
Fetal losses	523	605	698	565	290	1,760
Amnios/DS	190	190	150	120	70	320
Total cost ($x10^6)	105	125	178	168	100	383
Cost/case ($x10^3)	190	190	190	180	110	350

Age ≥35 and Age ≥30 = Screening based on maternal age
MSAFP <35 = Maternal serum alpha-fetoprotein screening, restricted to women <35 years old
AEH <35 = Multiple marker screening restricted to women <35 years old
Age ≥35 mix = AEH screening and age screening both offered to women ≥35 years old; two-thirds choose amniocentesis directly -- one-third choose AEH screeing

Guidelines for Genetic Laboratory Practices: Newborn Screening

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Newborn screening has existed for over 30 years in the United States and yet a unified national program does not exist. State programs function independently and are molded, in many instances, by geographic, political, and economic factors. In order to improve national practices, the Maternal and Child Health Bureau, U.S. Department of Health and Human Services, and the Council of Regional Networks for Genetic Services (CORN) have taken a leadership role in developing guidelines for successful newborn screening systems.

In its 1992 U.S. Newborn Screening Guidelines [1], the Newborn Screening Committee of CORN defined newborn screening as, ". . .an essential preventive public health program for early identification of disorders that can lead to potentially catastrophic health problems." It was further emphasized that the efficient and productive outcome of newborn screening depends on, ". . .the smooth integration of specimen collection, laboratory analysis, follow-up contact, and effective treatment." "Newborn screening is a system that includes private medical practitioners, laboratory personnel, administrative follow-up personnel, tertiary care centers, third party payers, and others with the same ultimate goal. This system must be designed to function smoothly and efficiently within the governmental/political framework which gives it life [1]."

Currently there are 53 programs that comprise the U.S. screening community including 50 states, the District of Columbia, Puerto Rico, and the Virgin Islands. All 53 screen for congenital hypothyroidism and phenylketonuria. Other disorders included in those screening programs are sickle cell disease (46), galactosemia (45), maple syrup urine disease (25), homocystinuria (21), biotinidase (17), congenital adrenal hyperplasia (15), tyrosinemia (6), cystic fibrosis (3), and congenital toxoplasmosis (2) [2]. In addition, 48 programs participated in the CDC's Survey of Childbearing Women for HIV by unlinked testing of newborn screening samples. While this survey has now been suspended, it serves to illustrate the manner in which current medical science views newborn screening systems with respect to potential genetic and infectious disease information. The medical, ethical, and legal dilemmas faced by policy makers in newborn and other screening programs will be addressed by others in this publication.

The 53 screening programs, while oriented towards similar ultimate goals, are quite varied in their approaches. All but three, Vermont, Maryland, and the Virgin Islands, require that all newborns be screened for specified disorders. In Maryland testing must be *offered* to each newborn, while in Vermont and the Virgin Islands, it is completely voluntary (although many medical practitioners perceive that it is mandated). All but 7 programs (NE, SD, KY, LA, HI, CA, PR) utilize a single laboratory, either state or regional, and approximately 75% of programs are funded through a fee-for-service. All states offer some type of repeat testing, especially for infants tested very early or for whom definitive laboratory test results were not possible on first screening, and 11 programs routinely report that over 80% of their births receive second screens [3,7]. Despite these different approaches, all programs report a combined effort to reach in excess of 98% of U.S. births which translates to over 4 million infants

screened annually. Thus approximately 1,200 cases of hypothyroidism and 225 cases of phenylketonuria are detected annually. Of programs reporting data for 1992 [6], 1,523 cases of sickle cell disease were detected, along with 59 cases of galactosemia, 6 cases of MSUD, 14 cases of biotinidase, 81 cases of CAH, 16 cases of cystic fibrosis, and 12 cases of toxoplasmosis.

In order to encourage uniformity of infant care and improve screening systems across the country, the Maternal and Child Health Bureau has provided support for a consultative review team to assist programs by assessing their laboratory, medical, administrative, and quality assurance procedures [8]. This team and the CORN Newborn Screening Committee published guidelines [1] for programs concentrating on eight major areas of concern: organization and administration, selection and evolution of disorders for screening, communication, quality assurance, funding, diagnosis (including management, treatment, and counseling), program evaluation, and liability. Included in these guidelines were suggestions regarding screening legislation and policies, formulation of advisory committees, selection of screening disorders, computerization, education, utilization of medical care providers, patient follow-up and tracking, counseling, and funding.

In addition to these general program guidelines, CORN has collected and published national newborn screening data since 1988 [3-7]. These data provide the most comprehensive national information available regarding program scope and case detection. This effort has now been joined by the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD) in an effort to assist in improving the quality of the data collected. CORN and ASTPHLD have also combined newborn committee activities in the assimilation of consensus information in an effort to encourage national standardization in a number of key newborn screening areas. Initial standardization efforts are targeted towards terminology, dried blood spots (retention, storage, usage), selection of newborn screening parameters, early discharge and timing issues, follow-up issues, specimen submitter guidelines, data collection (forms and format), proficiency testing and quality assurance, filter paper issues, and data management.

Newborn screening is a model program of the success that can be achieved in a massive public health effort aimed at improving the well-being of children affected by certain genetic disorders. It is so successful, in fact, that it is viewed as routine by many and often overlooked by bureaucratic administrators considering other public health problems that could benefit from its example, such as childhood immunizations. In order to improve our current newborn screening systems, programs are constantly advancing in automation and strategies for improved patient treatment and family services. Some programs have electronically linked hospital admission records for the newborn to birth certificates, insurance claims, and newborn screening specimen submissions and test results. Newborn screening programs have also taken a strong position on improving maternal and infant care through preparation of a consensus statement on the adverse affects of early hospital discharge following birth [9]. The follow-up/administration challenges facing programs screening for sickle cell disease are also being addressed by the newborn screening community in national conferences and through the CORN Sickle Cell, Thalassemia, and Other Hemoglobin Variants Committee.

It is clear that the future of newborn screening programs include increased use of DNA analytical techniques. Not only is DNA important in confirming results of test for disorders currently included in newborn screening programs, such as sickle cell disease and cystic fibrosis, but it also offers possibilities for program expansion [10]. As molecular biology and genetic treatment strategies progress, the definition of newborn screening will also change. It will be important to maintain a public health focus in our definition lest we lose sight of the reasons for newborn screening in a volatile legal/ethical/political climate. Perhaps the definition that will evolve will be a statement such as, "Newborn screening is a system of identifying genetic and other health problems in newborns and other family members that leads to overall improvement in the public's health."

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Presymptomatic and Predisposition Genetic Testing for Disease and Its Policy Implications

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Recombinant DNA technology and the Human Genome Project have brought us more than a full helical turn in genetic testing. The first tests identified women at risk of having fetuses with Rh incompatibility and newborns with phenylketonuria (PKU). Only a handful of diseases, in which secondary genetic changes could be detected in readily accessible tissues, were amenable to the technology of the time. With the new technology, tests can be devised for virtually any single-gene disease. In addition, we can test for genetic predispositions. In contrast to presymptomatic testing for single-gene diseases, in which a confirmed positive test result carries almost a 100 % chance of getting the disease, predisposition testing for multi-factorial diseases carries risks of less than 100%[1]. At the moment, predisposition testing is generating the most intense interest as development proceeds on predictive tests for coronary artery disease, breast and colon cancer, and Alzheimer disease.

The Draft, "Guidelines for Clinical Genetics Services for the Public's Health," prepared by CORN collaborators, uses the BRCA1 gene as one illustration of what is entailed in educating the public about a genetic predisposition. In the first part of this paper, I use this illustration to point out some common misbeliefs about testing for genetic predispositions[2].

The source of support for new genetic services is changing rapidly, as I discuss in the second part of the paper. Today's promotion of genetic tests by the biotechnology industry contrasts with the days when public subsidies (like the ones that established CORN) were needed to spur the availability of genetic services. Another change is the rise in managed care and the greater difficulty of referring patients to specialists. Consequently, a higher proportion of genetic services (including testing) will be in the domain of primary care providers. These changes pose new possibilities for genetic services, and new problems. They are particularly acute for predisposition testing, which may become the most frequently offered genetic service. The Task Force on Genetic Testing of the NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research is in the process of establishing principles for the development and delivery of genetic tests. In the third part of this paper, I summarize the work of the Task Force. In many respects, the principles being developed by the Task Force complement the CORN Guidelines, which focus on services already being delivered.

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[1]Author's Note: Tests offered to population subgroups, without regard to family history, are genetic screening tests. The term genetic testing is used to define all types of testing and also testing in high risk families.

[2]Editor's Note: The CORN "Guidelines for Clinical Genetics Services for the Public's Health" have been revised since the time of Dr. Holtzman's presentation.

Propagating Misperceptions About Genetic Predispositions

According to CORN's draft Guidelines, there are three "levels of sophistication" in educating the public: awareness, information, and instruction. To illustrate these levels, the Guidelines use BRCA1 as one example.[2]

> Level 1: "AWARENESS...BRCA1 is a recently recognized breast cancer causing gene which might in the future enable the detection of some individuals at risk for developing breast cancer."

Is BRCA1 a cancer-causing gene? We are doing a disservice to genetics education when we talk about genes causing disease instead of emphasizing that every gene has a normal function. Part of the confusion springs from our reluctance to use the terms "allele" or "mutation" when communicating with the public. We may think people cannot understand or are frightened by such terms, but their understanding is impaired and fear heightened by shying away from them. Part of the confusion also arises from the unfortunate habit scientists have of naming genes not for their normal function but for their dysfunction. BRCA1 has a normal anti-cancer-causing function, probably as a tumor suppressor.

Inherited mutations in the BRCA1 gene increase the risk of breast cancer, but do not cause cancer. Mutations in several other genes are needed before a breast cell undergoes malignant transformation. Women who have an inherited susceptibility mutation (ISM) at the BRCA1 locus require one less acquired somatic mutation for transformation. This explains their increased risk. Somatic mutations arise spontaneously or result from exposure to environmental mutagens. If the requisite number needed for malignant transformation don't occur, the woman will never get cancer.

> Level 2: "INFORMATION...BRCA1 has multiple changes within the gene, applies probably only to younger women of pre- or perimenopausal age, and cannot currently be used for presymptomatic screening."

What are "multiple changes"? Some people inherit or acquire a mutation that has the potential to alter or obliterate the expression of that particular allele. A susceptibility-conferring allele may not have multiple changes (deletion of one nucleotide can be sufficient) but the "change" in one person that increases susceptibility may be different than the "change" in another person, yet both changes have a carcinogenic effect.

As malignant transformation is a "multi-hit" process, the "hits" can accumulate over a woman's lifetime. The changes are not limited "to women of pre- or perimenopausal age." Women with an ISM will get breast cancer at an earlier age than women without one, but even among those with ISMs at the BRCA1 locus about half get cancer post-menopausally.

Why can't BRCA1 currently be used for presymptomatic screening? Companies and even some academic laboratories are already offering tests for BRCA1 mutations. Could there be problems with the test? If so, why can't the public be told what they are? The third statement, at the most sophisticated level, is no help:

> Level 3: "INSTRUCTION...the state of the art of BRCA1 screening, who gets it, what results can be expected, what is their significance, what is the molecular structure, etc."

Why not add "what the risks are"? To a person considering testing, is "molecular structure" more important then the disadvantages? Taken together, the 3 statements do not convey a balanced picture of benefits and risks.

Getting New Tests to the Public

More than any other specialty, medical genetics has relied on government support for its clinical development. Newborn screening and some forms of carrier and prenatal screening were, and remain, subsidized and are sometimes performed in health department laboratories. State and Federal funds continue to be used to support satellite clinics and to spread the word about genetics. Three inter-related reasons explain this unusual history. First, newborn screening for phenylketonuria (PKU)--the earliest genetic service to receive widespread government-support (and even be mandated)--could only be of benefit if performed in a very narrow age window. Second, most doctors caring for infants were slow to adopt screening, perhaps because the benefits were not established at the time screening started. Third, political pressures--largely in response to physician reticence--not only led to mandated screening but the establishment of laboratories and administrative units to handle newborn screening. Looking at each of these three reasons in the context of testing for genetic predispositions reveals changes in the factors needed to bring new tests to the public.

The narrow window. The age window for predisposition testing is wide open. Unlike PKU, we do not yet know when treatment has to be administered to prevent cancer or other adult-onset disease in those with ISMs. With few exceptions, as in familial adenomatous polyposis and familial medullary thyroid carcinoma (for which surgical extirpation is the treatment), we do not even know what treatments can prevent the disease. In the face of uncertain benefit to risk ratios, it would be inappropriate to commit public funds for providing services or mandating testing.

Physician reticence. When neonatal screening for PKU became possible, few physicians, including pediatricians, had ever encountered a child with PKU. They certainly have encountered the common disorders for which genetic predispositions are being discovered. These discoveries are often accompanied by claims that tests to detect those at risk are just around the corner. Medical journals and the popular press are full of stories about genetic discoveries. Increasingly, patients are asking their primary care physicians what can be done to detect those at risk and improve their outcome. Physicians may not have the expertise to answer these questions, but they will learn quickly.

Political pressure. With the discovery of recombinant DNA technology, research into genetic factors in disease escalated several-fold among academically-based investigators. The biotechnology industry developed in part because the new technology could provide previously undreamed diagnostic and, in some cases, therapeutic tools for which manufacturers predicted large markets. Commercial laboratories have already captured a good part of the"market" for biochemical and cytogenetic tests which, a few short years ago, were the exclusive province of academic and health department

laboratories. They are eager to develop tests for genetic predispositions to common disorders. Many people with genetic predispositions will report that several family members have the disease in question. Consequently, entire populations do not have to be screened, although commercial laboratories might be eager to do so. Today, political pressure is needed not to ensure the availability of genetic services for common diseases, but to ensure that services are safe and effective, provided in laboratories of high quality, and offered in ways to increase understanding of the benefits and risks and permit autonomous decision-making.

Particularly for rare, autosomal recessive diseases, subsidization is still needed. The commercial market is too small to lure investment. Government-run and/or supported programs will be needed to assure availability and access, at least until tests capable of detecting multiple rare diseases on a single specimen are technologically feasible. Commercial interest will then increase.

The Task Force on Genetic Testing

The Task Force has developed principles and is currently preparing recommendations in three broad areas:

(1) Scientific validation. A major concern of the Task Force is that tests introduced into clinical practice should be adequately validated, or that protocols are in place to assure adequate validation. Validation extends beyond establishing the ability of a test to measure accurately that which it is intended to measure (analyte), but also includes establishing clinical sensitivity (how many patients who have an ISM and get the disease can be detected), positive predictive value (how many patients with a detectable ISM get the disease), and clinical utility (ability of the information to improve patient outcomes). Although FDA enforces regulations that require manufacturers of clinical testing kits to demonstrate how their kits satisfy these criteria before they can be marketed, enforcement is much more lax for laboratories that market testing services rather than kits. Marketing of test services is the predominant mode of entry of companies into the genetic testing arena today. The Task Force is working closely with FDA to rectify this imbalance.

(2) Laboratory quality. Although the Clinical Laboratory Improvement Amendments of 1988 (CLIA88) brought every laboratory providing clinical testing under federal control, the current provisions and enforcement of CLIA88 afford little assurance that genetic tests will be performed reliably or that a laboratory's interpretation of test results will be understood by providers and their patients. Working with HCFA and CDC, the agencies principally responsible for CLIA88, the Task Force is exploring options for strengthening the federal role. It is drawing in part on some strong state models, notably New York and California. The Task Force has already concluded that one strong national standard is better than 50 different state standards.

(3) Education and counseling. Starting with the premise that genetic testing will expand beyond the capacity of medical geneticists and genetic counselors to handle the demand, the Task Force has considered how best to prepare non-geneticist providers to offer genetic services. It is coming to the conclusion that the deficiencies in most providers' knowledge of genetics and genetic tests warrant requiring that they show sufficient understanding of the field before they order tests. This becomes

particularly important if the ability of primary care providers to refer to geneticists or genetic counselors is curtailed. It will then be important for genetic counselors and nurses with expertise in genetics, if not geneticists themselves, to become part of managed care organizations.

Recognizing that non-geneticist providers have not been schooled in the attributes of non-directive counseling, and that commercial pressure could also promote patient acceptance, the Task Force is very concerned that patient autonomy in deciding whether or not to be tested be preserved. This is particularly important when the benefit to risk ratio is unclear, or tilted toward the risk side, and when reproductive decisions are involved.

Conclusions

The draft CORN Guidelines lay out a blue print for genetic services. I am not sure that they adequately recognize the changing face of genetic services, specifically, the increasing role of commercial forces in developing genetic tests and of non-geneticist health care providers in delivering genetic services. Nor do they address adequately the growing pressure to test for genetic predispositions. CORN has an important role to play in assuring not only that providers and the public appreciate the value of genetic tests but also their risks. If anything, there is a greater need than ever before for public agencies to assure safe and effective genetic testing.

Defining Education as a Genetic Service

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It comes as no surprise that the Council of Regional Networks for Genetic Services' (CORN) Genetic Services: Guidelines for the Public's Health defines education as a genetic service. By highlighting the role of education in these guidelines CORN recognizes that education is an essential component of a comprehensive public health genetic services program. Education about specific aspects of genetics and related genetic services is the basis of the provision of genetic services to individuals, their families, as well as population-based screening programs. Education about genetics is also of great benefit to those involved in the planning, delivery, implementation, and monitoring of genetic services.

The need to emphasize genetic education in these guidelines becomes clear when one surveys recent genetic advances. New genetic knowledge and technology advances stemming from the Human Genome Project (HGP) and the field of medical genetics have already led to an explosion of new information. Some of the accomplishments of the past five years include the construction of detailed genetic and physical maps of the human genome, the development of new techniques for DNA sequencing and information transfer, as well as improved understanding of underlying pathogenetic mechanisms for a variety of medical problems. Although the ability to diagnose many genetic diseases far outstrips current therapeutic efforts, gene therapy is now a reality. Carrier testing and population-based screening programs for a variety of genetic disorders and one category of birth defects are now in place.

It is anticipated that our knowledge of the role of genetic factors in the so-called "common" disorders such as heart disease, cancer, and autoimmune disease will also increase. New genetic information will provide unprecedented opportunities for individuals and their families to make decisions about their own health as well as the health of their descendants. Innovative treatment modalities will be developed. The end result will be an ever increasing demand for genetic information and genetic services.

In order to meet this demand there is a need for all health care providers and the general public to become more informed about the new and emerging developments in the field of medical genetics.

How can we best meet this challenge?

Let's examine the issues. First, just as our understanding of human genetics is increasing, sweeping changes are underway which will continue to alter the delivery of health care services nationwide. Emphasis is and will continue to be placed on the provision of community-based, comprehensive, coordinated, and cost-effective health care services. General medical services will be rendered by primary health care providers. These include family practitioners, general internists, general pediatricians, general obstetrician-gynecologists, and nurse practitioners. Referrals to medical subspecialists will be curtailed.

Such shifts in practice parameters will increase the role of primary health care providers in the provision of medical genetic services. Most observers believe that in the twenty-first century not only will non-genetic medical personnel order most genetic tests but increasingly they will be directly involved in the care and management of patients and their families at risk for genetic disease.

As these changes occur, the role of medical genetic personnel as educators will increase. One reason for this is that the number of trained medical genetic health care providers is small. Genetic service providers include MD and PhD clinical geneticists, master's level genetic counselors, master's level and PhD nurse-genetic counselors, and MD and PhD geneticists who are primarily concerned with the provision of cytogenetic, biochemical, and molecular genetic laboratory services.

Although the nation's genetic workforce is close to 2500 certified members not all MD and PhD geneticists spend all of their time on clinical activities. Many focus primarily on research and/or on laboratory services.

Most clinical genetic personnel work in tertiary care centers and/or in large community medical centers. Some are in industry and a few are members of state health departments. The geographic distribution of clinical genetic personnel also varies. Some states such as California, Texas and New York have relatively large numbers of genetic health care professionals. Others such as Mississippi and New Mexico have a few genetic health care providers. Alaska has no state-based clinical geneticist.

Furthermore the number of new clinical medical genetic health professionals is unlikely to change. Grants or scholarships for post-doctoral training are in short supply. Impending changes in Medicare funding will also impact on funds for postdoctoral medical genetic education. In addition, emphasis is now being placed on reducing the total number of medical subspecialty residents while increasing the number of primary care providers. Residency programs in pediatrics, internal medicine, obstetrics and gynecology, and family practice will train more generalists. This means that the number of subspecialists will decline. As a newly recognized medical subspecialty medical genetics will have to work hard to obtain slots in an institution's training program.

If and when these changes are implemented the quality of graduate education at all major medical centers will be affected. The potential impact on medical student and general residency training is hard to assess. Certainly resident/medical student teaching would be affected by the loss of genetic fellows.

There will be an ongoing need to train new leaders and teachers in genetics. Efforts must be made to find funds to educate a cadre of highly skilled medical genetic health care professionals. Such individuals will be needed to address patient and laboratory needs as well as to meet the genetic education needs of the nation's health care workforce.

Why is this important? There are few studies on the genetic knowledge of primary health care providers. The available surveys reveal major gaps in the participants' fund of genetic information.

Sponsored by the Genetic Services Branch, Maternal and Child Health Bureau (MCHB), pilot projects are now underway to more fully document the need for genetic education among a variety of primary health care providers. A major goal of these projects is to develop working partnerships between community-based primary care providers and local medical genetic personnel in an effort to pinpoint needs and to design and develop cooperative educational programs which can be implemented and field-tested within a variety of community-based settings. Some of the projects are developing innovative medical genetic curricula including telecommunication programs. All programs include rigorous evaluation components. For example, one program is assessing the impact of its educational program on its participants' practice parameters and the enhancement of the working relationships between the community-based practitioners and their local genetic service providers.

These programs are designed to be replicated with appropriate modifications in order to reach large numbers of primary health care providers within each MCHB-funded regional network. These projects will provide needed data on how to make genetic information more accessible, relevant, and user friendly.

Although we are now in a period of transition with respect to the delivery of health care services, it is essential that education be an integral part of genetic services. It is an essential service because it ensures our ability as clinical geneticists, public health providers, and concerned consumers to maintain an ethical framework for the delivery of genetic services.

Without an understanding of the facts, principles, and the language of genetics how can individuals and families seeking and/or in need of genetic services understand the information being exchanged, make truly informed individual decisions/choices, or select meaningful options? Medical genetic personnel and concerned consumers must maintain an ongoing dialogue with primary care providers and health administrators about such issues as patient autonomy, informed consent, confidentiality, non-directiveness, and directiveness to name a few. In turn medical genetic personnel will increase their knowledge of primary car including its strengths and problems.

High priority should be given to public education. Concerned citizens need to be exposed to balanced presentations about the new genetic advances as well as ongoing genetic service programs such as newborn screening. They need to understand the role of genetics in public health and vice versa.

Lastly some of CORN's educational efforts will need to be directed at health care policy makers at both the state and federal level. Policy makers need to be educated about the implications of the new molecular genetics as well as the spectrum of available genetic services.

One goal would be to increase the genetic knowledge of policy makers in order to facilitate the timely incorporation of medical genetic information and technologies along with the necessary genetic services into the nation's rapidly evolving health care systems.

As recognition of the role of genetic factors in all aspects of human development, health and disease expands, we need to continue our educational efforts about our field and its achievements at all levels. CORN will continue to play a leading role in genetics education because of CORN's unique public health perspective.

Genetics Education: Guidelines and Resources for the Public Health

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The field of human genetics is experiencing an information explosion: genes are cloned for the first time daily; new syndromes are recognized at a rapid rate; and clinically relevant laboratory tests are developed and then improved before the initial report can be published. At a time when experienced genetics professionals themselves are having difficulty "keeping up", non-genetics professionals and the public are understandably confused about what they should know. Educators in regional genetics networks are inundated with requests to teach. But what to teach, and to whom? Guidelines for health promotion education, developed within a public health environment, can help to answer these questions. Such guidelines take into account the needs of communities; once these needs have been identified, the vast resources available to genetics educators can be used for the development of programs which (1) meet documented community needs; (2) meet standards of accuracy; and (3) influence behaviors toward improved public health.

Guidelines for Public Health Educators

Health promotion is a function of public health systems. As participants, either formally or informally, in public health activities, geneticists can offer a variety of educational programs (including on-line services and telecommunication programs) which respond to the public's need for preventative, population based services. In so doing, adherence to guidelines and principles developed by public health programs is appropriate. This discussion is based on such guidelines, entitled "Standards for Excellence in Health Promotion Practice", developed by the Texas Department of Health. These standards assume that health promotion programs, including educational programs, will be community focused and responsive to the unique needs and characteristics of particular communities. The over-riding goal of such programs developed by geneticists is the prevention of the occurrence of genetic disorders where possible; when prevention of the disorder is not possible, then reduction of morbidity is the goal. These goals are met most effectively when efforts include patient and family education to enhance understanding of genetic disorders and their treatment.

The tasks which are outlined for the development of an excellent program are not trivial; they require a substantial investment of time and effort for program implementation. They also require evaluation for program effectiveness and impact. However, if the efforts of skilled professionals are to be expended on such programs, and particularly if public dollars are needed to produce such programs, then this kind of comprehensive approach is warranted.

Data Collection

Educational programs are most effective when they are provided in response to perceived or identified community needs. Whether educational programs target the general population within a community, or certain health care providers within the community, knowledge of community needs will permit the educator to focus the program on issues which are perceived by the public and the health care

professionals as requiring action. In some instances, the community may be unaware of a problem which requires attention: Data collection can then identify the need for action in a manner which is convincing to the community. In the context of this discussion, a community may be a circumscribed neighborhood or a much larger geographical region, such as a state. Alternatively, a community may represent a segment of a population within a geographic region, such as members of a particular ethnic or racial group, individuals with a particular medical condition, or individuals at risk for a particular disorder. Whatever the definition of community, an educational program will be most effective when it is developed with consideration for the following variables: community resources, power structures, vital statistics, demographics, health status, community dynamics, and the social, cultural and environmental characteristics of the community. Such data frequently can be obtained from vital statistics, census data, public documents, and observation. Data should be collected based on principles of epidemiology, demography, and the social and behavioral sciences.

Diagnosis of the Community's Assets and Needs

In partnership with the community, the following parameters should be evaluated: availability of services, mortality/morbidity rates, specific populations at risk, health promotion needs of the community, community processes, leadership, and education.

Planning

This process is based on the assumption that specific educational programs will be developed which are appropriate to a particular community and the needs of the individuals who live within it, and are reflective of the information obtained from the data collection and community assessment processes. Community participation in the planning process is important. Program planning should include development of the following: (1) measurable goals and objectives, with an expected date of accomplishment where appropriate; (2) an identifiable sequence of actions for achieving the goals; (3) identification of resources necessary to achieve the goals; (4) estimates of costs and benefits of the plan; (5) opportunity for revision of the plan as goals and objectives are reached or changed; (6) a method for establishment of priorities.

Intervention: the Educator Educates

To ensure a successful program with appropriate content, it is assumed that the educator is a credible expert. The earlier processes of data collection, diagnosis, and planning ensure partnership with the community in the educational process. The focus of the program may include health care providers, community leaders, teachers, librarians, and/or organizations for implementation of future programs and development of resources. Success of the program will be enhanced if the following additional criteria are met: (1) the content of the program is reviewed and revised, based on community response; (2) culturally appropriate methods and media are used; (3) current technologies are emphasized; (4) principles of community organization are considered when it is necessary to develop community resources; (5) implementation of interventions takes into account the participation of individuals and families; (6) collaboration with community health programs is emphasized; (7) genetic services are coordinated with other health services; (8) mechanisms are included to inform the community about health status and resources; (9) preventive concepts and skills are taught.

Evaluation

To justify the expenditure of resources for educational programs, it is necessary to show that such programs are accepted by the community and result in progress toward a goal or goals. Under ideal circumstances, information from the practice setting will be available to determine such progress. The evaluation process should fulfill the following criteria: (1) it is ongoing, timely, and comprehensive; (2) baseline and current data are used to measure progress toward a specific goal: (3) priorities, goals, and interventions are revised to reflect the results of the evaluation process; (4) results are communicated to other educators and decision makers; (5) there is a process of peer review.

Interdisciplinary Collaboration

Genetics education programs are intended to meet specific goals for prevention and reduction of morbidity. To be effective, educators will need to collaborate with other professionals and community representatives in assessing, planning, implementing, and evaluating these programs. The importance of public education cannot be overemphasized; frequently, public awareness will encourage professionals to proceed with a program.

Structure of Educational Programs

To improve the public health, genetics education must be provided at different levels of sophistication to a wide variety of target audiences within communities. Laxova et al. (Guidelines for Clinical Genetics Services for the Public's Health) have identified three levels of education in which participation by public health systems is appropriate. These are: (1) awareness, in which a broad target audience is made aware of the existence of a subject through flyers, posters, television public service announcements ,and the like; (2) information, in which teachers, non-genetics health professionals, consumers, interest groups, and media personnel are educated through such mechanisms as workshops and brochures; and (3) instruction, in which providers, MD specialists, support groups, consumers, educators, and others with particular interest in a subject receive in depth information through workshops and conferences. Each of these types of programs deserves the planning, implementation and evaluation processes described earlier if success is to be demonstrated.

Resources for Genetics Education

The Council of Regional Networks for Genetic Services (CORN) has developed a publication entitled "Directory of Educational Resources in Genetics: Organizations and Databases". This publication lists a broad range of resources for the development of educational programs and is appended. Importantly, the vast increase in genetic information currently available at hundreds of World Wide Web sites on the Internet expands the avenues and compounds the problems of providing accurate information in a timely manner for specific communities.

DIRECTORY of EDUCATIONAL RESOURCES IN GENETICS: ORGANIZATIONS AND DATABASES

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TABLE OF CONTENTS

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Making Genetic Services and Education Culturally Relevant

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Introduction

In recent decades, it has become increasingly clear that health education must be an integral part of all health services. In the practice of clinical genetics, services and education are in fact inseparable because without a sound understanding of the basic terminologies, facts, principles as well as the social, ethical, and legal implications of involvement with genetic service, one can hardly make true informed choices or decisions. And making important decisions about one's own health without being fully informed seriously compromises one's autonomy. Stated simply, offering genetic testing or other services without adequate prior education virtually assures a direct violation of the widely held ethical principle of voluntariness and personal autonomy in the utilization of genetic services. Well-planned genetics educational programs for the public are therefore essential if advances made by the Human Genome Project are to be translated realistically into meaningful services. But education of the general public is not enough. Intense educational effort must also be aimed at the non-geneticist health workers, particularly the primary care providers. As the explosion of scientific knowledge and technology in the field of genetics continues, primary care providers will become increasingly involved in offering genetic testing and some type of counseling. Yet few are prepared to offer such services.

Turning to the topic of my presentation - Making Genetic Services and Education Culturally Relevant, perhaps we can begin by asking this question: why should culture be considered in genetic or any other types of health services and education? To answer this question, let us examine the definition of health itself, since the ultimate goal of all health services, including genetic services, is to improve the health of those who are served.

Health: A Culturally-bound Concept

Health is a word that is frequently used but seldom defined. The assumption is that everyone knows what health is. While this assumption is correct, few may have ever stopped to ponder over the fact that health is a culturally-bound concept; the same word can have very different meaning for different people, particularly for people from vastly different cultures. The World Health Organization defines health as "a state of complete physical, mental and social well-being, and not merely the absence of disease." This concept is widely adopted by health care systems and professionals in the Western industrialized world. But for people from other cultures, such as some Native Americans, health is a state of physical and spiritual harmony with nature. To still others, health is quite simply the absence of illness, and one who feels fine is healthy. In a culturally pluralistic society such as that in the United States, the word "health" often means very different things to different people. It is therefore critical that health professionals recognize that **health is a state of well-being that is culturally defined, valued and practiced** as noted by Leininger. Understanding this key fact is an essential step toward effective health education and services because in a culturally diverse society, a monolithic health care system cannot meet the needs of all its populations.

Culture: Its Influence On Health Beliefs and Behavior

In order to understand the influence of culture on health behavior, we should first examine briefly what culture is. Anthropologists differ in their definition of the word, but put simply, culture is a system of learned behavior, or standards for perceiving, believing, evaluating, judging and acting that one acquires as a member of a society. It defines the rules for appropriate behavior by which people assess themselves and others. It also provides the value system used in determining the importance and relevance of events based on which decisions are made. In societies with a relatively homogeneous population, the existence of culture may be easily overlooked. But in a heterogeneous society, the influence of culture on health concept, belief, attitude, behavior, and other aspects of life becomes much more apparent. Even so, the significance of culture in health behavior is often overlooked.

Here in the U.S. where one in every four persons is a racial or ethnic minority (black or African American, Hispanic, Asian and Pacific Islander, American Indian and Native Alaskan), ethnocultural barriers to genetic and other health services present a serious problem which has yet to receive its due share of attention. While linguistic barriers, which are much more obvious, are generally recognized as a common problem for certain populations, ethnocultural barriers tend to be more subtle and easily missed. The latter are often overlooked in people without overt language difficulty. But culture in fact influences not only how one defines health, but also what one believes about disease causation and manifestations; terms one uses to describe certain symptoms; how one behaves during illness; when, where and how one seeks help; what types of treatment one expects; and whether one is inclined to follow prescribed procedures or treatment. Culture also dictates who in the family is responsible for decision making and what is the proper standard of behavior in interpersonal transactions such as that between physicians and patients.

Culture not only determines individual attitude and behavior toward health, it also shapes the health care system. The U.S. health care system today is a cultural system designed and administered largely by mainstream Americans for mainstream consumers, and until recently, the system gave little consideration to the cultural diversity of the population it serves. It is important to acknowledge that the biomedical model which forms the basis of the Western health care system is not necessarily familiar to or embraced by people of all cultures. Some racial or ethnic minorities as well as new immigrants may have very different concepts and beliefs about the causes of their illnesses and expect very different treatment. Health care systems need to acknowledge these differences and make their services more culturally sensitive and relevant to the population they serve.

Some Cultural Considerations in Genetic Services and Education

Knowledge that certain diseases run in families spans all cultures, but explanation for such occurrences may vary widely. For those who believe that diseases are punishments for misdeeds, such punishments may be viewed as having been imposed on descendants of the "guilty party" for generations, thereby running in families. Where curse is held responsible for illnesses or unusual happenings such as birth defects, such powerful evil forces may likewise be viewed as persisting for generations affecting many members of the same family.

Beliefs about the causation of illnesses are directly linked to one's attitude and approach to the problem. For example, when illnesses are viewed as a punishment for misdeeds, shame is an overriding concern for the affected family, and such "disgraceful" happenings are not to be shared with outsiders. Important genetics information may thus be purposely omitted or even denied in family history or personal medical history. Moreover, medical intervention may be perceived as interference with one's destiny that could bring on more severe forms of penalty, and should therefore be avoided. For some, the mere mention of diseases or mishaps is believed to bring about such happenings. This belief may translate into reluctance, for example, to be engaged in discussions about prenatal screening for certain disorders or presymptomatic screening. For those who equate health with the absence of illness, presymptomatic screening of apparently healthy people makes little sense.

In addition to its influence on health behavior, culture also determines a person's position and responsibilities in a society. In some cultures, a woman is held solely responsible for the outcome of her pregnancy, including the sex of the child she bears. Yet she may have little autonomy over her personal life, including her reproductive life. In cultures with strong family-orientation, the decision-making process for what may seem to be a simple personal matter may involve many family members, particularly those with authority such as the elderly. In such cases, genetic counseling that targets only women and their partner may have little practical impact on the decision-making process.

In reaching out to persons of non-mainstream cultures, it is also important to understand the influence of culture on interpersonal transactions. In many cultures, respect for authority figures such as health professionals means not looking straight into the person's eyes - a behavior often misconstrued as inattention or avoidance in an effort to hide something. Likewise, asking question or seeking clarification is considered by some to be disrespectful and even rude. For those from cultures in which authority figures are expected to be clearly directive, the emphasis on non-directiveness in genetic counseling can be very confusing and troubling. Individuals from backgrounds where personal autonomy and informed decisions are not part of the common vocabulary may find such discussions barely intelligible.

Responding to Cultural Diversity in the United States

For health professionals with little exposure to racial and ethnic minorities or recent immigrants and refugees, the above presentation on non-mainstream health beliefs, attitude and behavior may appear to have little relevance to the delivery of genetic services in modern day United States. Yet one must not forget the fact that the U.S. is a land of people from many lands, a nation of people from many nations. In 1990, 8 percent of the U.S. population were foreign-born; 14 percent of persons 5 years or older spoke a non-English language at home; 3 percent either did not speak English or did not speak English very well. While most persons with linguistic barriers are minorities, many are white and of European origin. In recent years, many refugees and immigrants have come from the former Soviet Union.

Today, one in every four persons in the U.S. is a racial or ethnic minority, and cultural diversity has become an ever-expanding phenomenon in this country. During the past quarter of a century, minorities have grown at a rate three times that of the total population. Between 1980 and 1990, minorities

increased by 32.5%, the total population by 9.8%, and whites by only 6%. In the 1990 census, blacks, Hispanics, Asians and Pacific Islanders, American Indians and Native Alaskans totaled more than sixty million. Although minorities accounted for 25% of the total population, they were responsible for 67% of the intercensus increase of the total population.

The dramatic rise in minorities in recent decades reflects the relatively young age structure of these populations, a higher fertility rate, and a change in immigration pattern. During the past half a century, there has been a steady decline in immigration from Europe and a sharp rise from Latin America and Asia. The latter two regions now contribute to about three quarters of U.S. legal immigrants. Resettlement of two large waves of refugees from Cuba and Southeast Asia contributed further to the increase in Hispanics and Asian Americans. The U.S. Census Bureau projects that by the year 2050, non-Hispanic whites will make up only 52.7% of the total U.S. population; Hispanics will comprise 21.1%, blacks 16.2%, Asians and Pacific Islanders 10.7% and American Indians and Native Alaskans 1.2% of the population.

Making Genetic Services and Education Culturally Relevant

Given the current racial and ethnic composition of the U.S. population and the projected trend, health planners, including those responsible for genetic services, must make every effort to assure that health services are culturally relevant to the population targeted.

To overcome ethnocultural barriers to genetic and other health services, certain crucial steps must be taken. Health workers must recognize the very existence and influence of culture in their own lives, and examine their own cultural heritage and perspective. They must take a broader view of the world and acknowledge other cultures around them. Without taking these steps, the inevitable result is ethnocentrism, i.e., the assumption that one's standards or value system is the only one worthy of consideration, and useful as the norm for all others. Genetic and other health professionals also need to spend time learning about other cultures, learning to see the world as others see it, and learning to see themselves as others see them.

All genetics education and services programs need to be culturally sensitive to the population for whom the programs are intended. Since access to services is a particular problem for many minorities and new immigrants, every effort should be made to reach out to these communities and their leaders, and to earn their trust and cooperation. Consultations should be sought from the community leaders about the most appropriate media, approach, content, setting, location, time, and other details of educational programs. Assistance should also be sought from local ethnic newspapers, radio, and TV stations. Special effort should be made to listen to the target population's concerns and interests, and to learn about their concepts, beliefs, knowledge, and understanding of genetic disorders and current technologies without making any assumptions or judgments. Equally important is a demonstration of respect for other cultural beliefs and values even when one disagrees. Where certain cultural practices such as consanguinity are common, discussion and counseling about the associated genetic risk should be done with special cultural sensitivity.

In attempting to make genetic services and education culturally relevant, a major pitfall is the use of stereotypes. It is critical to understand that not all racial or ethnic minorities are outside of the mainstream, nor do all whites embrace the mainstream culture. Cultural insensitivity is painful, but stereotyping may be even more hurtful. Considerable intra ethnic variations exist in every population, and the degree of acculturation in minorities also varies widely. A third generation Mexican American is likely to be quite different from a recent immigrant from Guatemala, even though both are Hispanics. Likewise a fourth generation Japanese American probably has little in common with a recent refugee from Cambodia but both are classified as Asian Americans. In short, health programs, including genetics programs, cannot be successful without treating and respecting each person as an individual.

Conclusions

Culture plays a key role in determining a person's attitude and behavior toward health, and in shaping the health care system. Yet ethnocultural barriers to genetic and other health services have received only limited attention. Immigration has risen sharply since World War II, and, during the past 25 years, racial and ethnic minorities in the U.S. have increased at a rate more than three times that of the total population. Cultural diversity has become an increasingly visible phenomenon in the U.S. Today one in every four persons is a minority, and the rapid growth of minorities is expected to continue. Advances made by the Human Genome Project cannot be translated into meaningful human services without concurrent development of culturally sensitive genetics educational programs that target both the general public and non-geneticist health professionals, particularly the primary care providers.

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Should Genetic Health Care (GHC) Providers Attempt to Influence Reproductive Outcome Using Directive Counseling Techniques: A Public Health Perspective

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Abstract

Two widely expressed tenets of the prenatal genetic counseling process are: (1) providers should never attempt to influence the outcome of a pregnancy, and (2) providers should use only non-directive genetic counseling techniques. From a public health (PH) perspective, these tenets could be viewed in some instances as counterproductive, illogical, and contrary to a major goal of PH (i.e., to improve the health and well-being of all residents including newborns).

There are many areas of interest [e.g., the prevention of fetal alcohol syndrome (FAS), neural tube defects (NTDs), fetal rubella syndrome, etc.] which involve preconceptional and prenatal care that are of major concern to GHC providers (i.e., MD and PhD clinical geneticists, master's level genetic counselors, and others) and PH agencies. PH's message regarding FAS prevention is clear: If you are pregnant, don't drink; and if you drink, don't get pregnant. PH's message regarding NTD prevention is equally clear: the CDC has recommended that all women of childbearing age who are capable of becoming pregnant should consume 0.4 mg of folic acid daily to reduce the risk of NTDs. State laws and regulations regarding immunizations are well known and, potentially, they could be very effective in preventing a number of conditions including fetal rubella syndrome.

In the past, issues such as eugenics, therapeutic abortion of affected fetuses, and a lack of methods for the primary prevention of birth defects and genetic diseases have caused GHC providers to perform genetic counseling according to the two tenets mentioned above. Clearly there are no moral, ethical or legal reasons why children at risk for FAS, NTDs, fetal rubella syndrome, or other conditions should not have the opportunity to be born healthy. It is time for GHC providers to re-examine these tenets on a case-by-case basis to determine when it is appropriate to use directive counseling techniques to improve reproductive outcome in accordance with the goals of PH. A framework is provided here that we believe could serve as a guide for future discussions dealing with these issues.

KEY WORDS: genetic counseling, directiveness, pregnancy outcome

Introduction

Public health has long been recognized in Anglo-American law as a proper governmental function both as a moral duty and an economic benefit. From the 14th century, the government of London empowered medical professionals to oversee drug production and examine individuals who suffered from communicable diseases. During the Renaissance, quarantine was mandated by governmental entities from Venice to Sweden to protect the public's health. Active public health policy regarding sanitation and disease transmission was developed by individuals like Edwin Chadwick in England in the 1840s and

1850s. Sewers were closed and water supplies improved. Morbidity and mortality rates declined dramatically.

Active public health policy in the United States was observed in the forced isolation of "Typhoid Mary" and in denying public school admission to students without proper immunization. *Our government has long recognized that the rights of the many outweigh the rights of the individual if individual rights present a significant health hazard to others (e.g., sanitation, infectious disease control and prevention, environmental protection, licensing and certification, etc.).* Therefore, public health's long history has been consistent with an active, interventionalist philosophy, especially in the area of prevention.

Background

Genetic counseling has grown up against a background involving eugenics, which had strong racial and state sponsored human improvement overtones[1-3], and an acrimonious debate over abortion. Thus, it appears that to avoid tainting itself morally and politically, genetic counseling has been tied to two well known tenets: (1) providers should never attempt to influence the outcome of a pregnancy, and (2) providers should always use non-directive counseling techniques.[4-9] That these two tenets in the genetic counseling process have been strongly influenced by eugenics and the abortion debate is patent. More recently, influencing the outcome of pregnancy seems to be a rubric for abortion. Otherwise, it leads to medical absurdities. For example, a pregnant woman discovers that her fetus has a potentially lethal but *in utero* repairable defect. Are we to assume that it is responsible to present birth and death without repair as equivalent alternatives to a willing mother? In fact, such a situation, like heart surgery in adults, dictates presenting data for informed decision making, rather than non-directive counseling. The end result has been the creation of a philosophy in clinical genetics that is passive, non-interventionalist, and slavishly universal.

The medical literature is replete with information stating that GHC providers must provide counseling that is non-directive, supportive, responsive to the individual's requests, and respectful of the choices of patients and families.[10] In fact, GHC providers are not above the law and if, for example in Washington State, we discover during a patient/family genetic evaluation evidence of child abuse or neglect, we are obligated to report our findings to a child protective services agency, just like any other health care provider. Therefore, we suggest that genetic counseling might be seen better in terms of: (1) counseling which could end in terminating a pregnancy which, for moral and political reasons, should be non-directive and, (2) counseling to improve the outcome of pregnancies where abortion is not an issue. Counseling of this latter type is congruent with traditional and contemporary medical and public health concerns.[11-13] It seeks not only to educate the patient, but also to influence informed decisions on the part of the parties involved for their good, the fetus' good, and the good of society.

Ethical Principles, Values, and Goals Pertinent to Prenatal Genetic Counseling

If it is reasonable to assume that directive prenatal genetic counseling is appropriate when the expectation is that the pregnancy is going to be brought to term and where the best outcome for the fetus is in the interest of the mother, father, and society, we must examine examples for this type of prenatal

genetic counseling and how they relate to well known ethical principles, values, goals, and a process regarding the care of patients.

Ethical Principles and Values

Health care providers are supposed to abide by the following principles:

- autonomy - the obligation to respect the decision making capacities of autonomous persons who have been fully informed with accurate information
- beneficence - the obligation to provide benefits and to balance benefits against risks
- non-maleficence - the obligation to avoid the causation of harm
- justice - obligations of fairness in the distribution of benefits and risks

In the United States today, many individuals do not know that autonomy is, in fact, a double-edge sword that includes: (1) the freedom to act without external coercion and, (2) the capacity to accept responsibility for one's actions including being held accountable for one's own conduct. In our current litigious, "don't tread on me" society, the concepts of beneficence and non-maleficence have often taken a back seat to that part of the principle of autonomy that says, "I want the freedom to act without external coercion." While autonomy should be highly prized in our society, it is not the principle of greatest value in some situations. For example, if it is totally unacceptable for someone to give large quantities of alcohol to a five year old on a regular basis, why should it not be equally unacceptable to give large quantities of alcohol to a fetus who is going to be brought to term? *Therefore, in preventing birth defects that are readily preventable and when there is a low risk to the mother, we believe that it is everyone's duty to try to improve the outcome of a pregnancy when the expectation is that the pregnancy is going to be brought to term.*

Goals

The following goals of medicine (and public health) should help parents have healthy children and thereby benefit the child, family, and society:

- promote health and well-being
- prevent disease
- relieve symptoms, pain and suffering
- cure disease
- prevent untimely death
- improve functional status or maintain compromised status up to the point of merely prolonging death
- educate and counsel patients regarding their condition, its cause, treatment, prognosis, and recurrence risk

The ethical principles, values, and goals noted above support GHC providers in helping parents prevent certain birth defects and genetic disorders through directive counseling which allows autonomous parents to make informed decisions when the expectation is that the pregnancy is going to be carried to term. As our legal system, through Roe v. Wade[14] and sustained in recent cases like Planned Parenthood of Southeastern Pennsylvania v. Casey[15], places primary decision making power for the fetus with the mother, the counseling is aimed at the mother for the benefit of the fetus. The father is also a major player as he is legally liable to support any born child. *In our view, the autonomy of the mother is not abridged and the rights of the father are respected because in a pregnancy that is expected to be carried to term a focus exists on the welfare of the fetus in the hope that he or she will have the optimal opportunity to be born healthy.* This is in keeping with the recommendation of the President's Commission on Making Health Care Decisions (1980): "Competent persons should be permitted to make decisions based on their own personal values and in furtherance of their own personal goals."

The Concept of Duty as an Aid in Defining Ethical Requirements for Prenatal Care Providers

Although not all breaches of duty have an ethical dimension, the principles, values, and goals of health care noted above often create a sense of duty for providers that is ethical in nature. For example, the ability to cure or prevent disease creates a duty in the practitioner to inform the patient of such interventions, particularly if there is a low risk to the patient and a reasonable chance of success. Failure to do so is a breach of ethics. Patient autonomy begins once the provider's duty to inform is discharged. An awareness of such duties helps the provider determine his or her responsibility in the provider-patient relationship. The provider must also determine his or her duty and obligations, if any, to the public's health. In many aspects of health care, including prenatal care, duty and ethics go hand in hand.

Genetic Counseling: Its Goals and Process

The American Society of Human Genetics has defined genetic counseling as a communication process that deals with problems associated with the occurrence and recurrence of genetic disorders including multifactorial conditions caused by genetic and environmental factors.[16,17] The process includes helping families (counselees):

- comprehend medical facts, including the diagnosis, probable course of the disorder, and the available management
- appreciate how heredity contributes to the disorder, and the risk of recurrence in specified relatives
- understand the alternatives for dealing with the risk of recurrence
- choose the course of action which seems to them appropriate in view of their risk, their family goals, and their ethical and religious standards, and to act in accordance with that decision
- to make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.

In order to fulfill these objectives, the following process has been identified[18]:

- eliciting a complete individual and family social, reproductive, and health history

- risk assessment
- consulting with the individual and family about available clinical evaluation and testing options including risks, benefits, limitations, interpretation, and possible psychological and economic consequences of genetic testing and diagnosis
- a psychosocial assessment and intervention
- facilitating medical and reproductive decision making in a non-directive fashion
- anticipatory grief and crisis counseling
- facilitating medical screening, testing, or management options as requested by the individual or family.

A Proposed Modification in the Genetic Counseling Process

What we propose is a modification in the prenatal genetic counseling process involving pregnancies that are going to be carried to term. We encourage GHC providers to use directive prenatal genetic counseling techniques in appropriate situations, e.g.:

- educating and encouraging women in their childbearing years to supplement their diet with 0.4 mg of folic acid per day to decrease the risk of NTDs
- educating and encouraging women who have had a child with an NTD to take 4 mg of folic acid per day prior to and during the first trimester of future pregnancies to reduce the recurrence risk of NTDs
- educating and encouraging women with diabetes mellitus or PKU to adhere to therapeutic regimens before and during pregnancy to reduce the risk of birth defects
- educating and discouraging alcohol consumption in women at risk of becoming pregnant or who are already pregnant to prevent alcohol related birth defects
- educating and encouraging the referral of pre-pregnant, pregnant, and post-partum alcoholic women for participation in and completion of chemical dependency treatment services, especially in women who have already had a child with an alcohol related birth defect
- educating and encouraging childbearing age women and men who abuse alcohol and/or drugs to use birth control, especially in women who have already had a child with an alcohol related birth defect
- educating and warning women who are at risk of becoming pregnant or who are pregnant not to smoke, use Accutane (isotretinoine), or take excess amounts of vitamin A.

Parents, fetuses, and society benefit when medical knowledge is applied to prevent preventable birth defects. We know of no legal, political, or moral canons that are violated by practicing this type of directive prenatal genetic counseling. In fact, a sense of duty provides support for using directive genetic counseling techniques in some situations.

We fully understand that GHC providers are supposed to support decisions made by autonomous parents, but we do not believe that unconditional support should be given to mothers who, for example, drink and/or smoke during a pregnancy or fathers who do not provide a healthy, supportive environment. We also recognize that there are patients who could be offended by such recommendations or who will

cut off their noses to spite their faces and their children's faces, even though they have been advised not to do so. However, there is sufficient information in the medical and health care literature which strongly supports the notion that patients can change their behavior if directive counseling techniques are used.[19] In this way, counselees will be treated as individuals and provided information according to their needs and obligations while infringing as little as possible on their autonomous decision-making power and responsibility.

Conclusion

The patient-genetic health care provider relationship is more than one of an expert with special knowledge that the patient is seeking. We believe it is a fiduciary duty of a GHC provider to make specific recommendations (i.e., to provide directive counseling) in certain situations. A provider who fails to attempt to persuade his/her patient to avoid a known teratogen during pregnancy, or to take an essential medication like folic acid prior to conception and during early pregnancy, is failing in his or her duty and may incur legal liability. In such cases: (1) the actions we are suggesting are aimed at an important goal, (2) there are no simple alternatives that can realize the goal of preventing these preventable birth defects, (3) the degree of infringement on the principle of autonomy is minimal, and last but not least, (4) there is a significant chance that reproductive outcome will improve. Furthermore, as we gain new information in the future, we should expect that there will be additional issues and conditions that will require the possible need for directive counseling to prevent other preventable birth defects and genetic diseases.

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Current Research and Future Directions for Genetic Services

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I would like to describe to you what the impact of the human genome project is going to be on medical genetic developments with particular reference to your interests, and to tell you the good news and the bad news.

The good news is that the current explosion in information is going to increase markedly our understanding of genetic disease and our ability to identify predisposition to genetic disorders. We will be able to provide counseling, non-directive or directive, to deal with this.

The bad news is that we are going to have an explosion of information which is going to allow us to diagnose genetic disease and predisposition to genetic disease, and provide counseling, either directive or non-directive for people who are being studied. The reason for that being the bad news is the issue of who is going to provide these services, how are they going to be provided, who is going to pay for them, and how does society feel about dealing with these issues.

Dr. Davis has already mentioned one other theme that I'd like to repeat; that is, I think that the Maternal and Child Health Division through its Genetic Branch has been very active in the genetic services area with its focus on maternal and child health, and that is absolutely appropriate. They should be continuing that in an even more expanded way -- if the government sees the wisdom of that happening. But we also need to consider adults. A great deal of what is going to be developing over the next few years will pertain to adult disorders and predisposition to disease rather than to prenatal problems or birth defects. We are going to have to have a more concerted effort joining the people in maternal and child health with people who are involved with cancer and cardiovascular disease, psychiatric disease, and a variety of other areas. All must join forces to provide genetic services in a much broader way.

I strongly believe that genetics has become the central science of medicine and that virtually all disease, except perhaps trauma, has a genetic component. For this reason, genetic research is going to have an impact on every aspect of medical care. We now know fairly clearly that the presence of disease is the result of a genetic predisposition, which can either be a single gene or multiple genes acting together and affected by environmental factors, the nature of which we are only now just starting to be able to dissect.

On the one hand, it is this interaction between genetic predisposition and environmental factors which makes the situation very complicated, but, on the other hand, environmental factors are elements that we can manipulate through medication, diet, lifestyle, and a whole variety of other approaches. This is a source of tremendous hope for our ability to intervene in ways that could be very helpful to people who are predisposed to genetic disorders. As the genome project proceeds and we learn more about genetic predispositions, we are going to see that we all have predispositions which, when influenced by the environment, can have a negative impact on our health.

I would like to discuss where human genome research has been and where it is going. Up until about ten years ago, the basic paradigm for the identification of genetic disease was the following: (1) start with a disease like phenylketonuria, (2) search the patient's blood, urine, or other tissues for some clue as to what might be abnormal. In this example, abnormal phenylalanine metabolites, phenyl ketones in the urine, provided a clue that the defect involved the biochemical handling of phenylalanine. From there you then (3) work back through the enzyme that is defective to the gene that is encoding that enzyme, phenylalanine hydroxylase, in the liver. As a last step (4), perhaps almost as an afterthought, you find out where on a chromosome this gene is located. This approach has been called functional cloning. It means identifying a gene through a knowledge of the defect or the pathophysiology of the disease in question. Functional cloning has been the way almost all genetic diseases have been identified up until approximately ten years ago.

A powerful alternative approach, termed positional cloning, has been developed over the last ten to twelve years. In positioning cloning, we begin with a disease whose underlying pathophysiology is unknown. Usually there have been decades of research studying patients' blood samples, urine, and a myriad of other tissues in a frustratingly unsuccessful attempt to identify the basic molecular defect that is causing the disease. Positional cloning lets us take an alternative approach where we begin by assuming that the disease has a hereditary component. We then proceed to map that disease without knowing anything about the gene or what the defect is. Once we have an approximate gene location, we then search that region for all the genes that are known to be located where we think the disease gene is. We then study these candidate genes by carefully looking for alterations, and often sequencing the gene. From the knowledge of the structure of the gene, we try to infer the function of the encoded protein and how alterations in that protein produce the disease in question. This approach uses a completely different paradigm for identifying disease genes -- not based on what a gene does (functional cloning), but where it is (positional cloning).

It follows that if we want to know where something is, we need maps. We have a chromosome with DNA and a gene and a protein. Each chromosome contains thousands of genes, and altogether we estimate that a set of human chromosomes contains perhaps 100,000 genes, although those estimates may be off as we learn more. How do we find where a disease gene is located if we do not know what the gene looks like? We find it through a two-step process. The first step uses genetic linkage maps or genetic distances, and the second relies on actual physical maps of the DNA. We actually have fragments of DNA called markers, which are connected in a way that allows us to identify a chromosome region where a certain disease gene may be located. We can map disease genes in families without knowing anything about the disease gene itself if we follow the inheritance of these DNA markers. We can just search through the genome using all the markers that are stretched out along all the chromosomes, and simply ask the question over and over again: when you inherit the disease, do you always inherit one of these particular markers, and if so, which marker is that chromosome on? If we find a DNA marker that is passed on with the disease, then we know that particular DNA marker is close to the actual gene for the disease. Since we know where the marker is located, we know the chromosome location of the disease gene and we can begin an intensive search in that region for candidate genes.

We need genetic maps and densely spaced DNA markers in order to be able to follow the inheritance of disease genes. The creation of these maps and closely-spaced markers has been a major function of the human genome project in its first five years. The goal -- and we're rapidly approaching that -- is a complete genetic map, with markers so densely spaced along the chromosome that the location of a disease gene can be pinpointed anywhere on the twenty- three pairs of chromosomes.

Once we have a genetic map with markers along the chromosome, we want to start creating physical maps. This just means isolating fragments of DNA between these genetic markers so that we actually have the DNA in hand in a test tube to be able to study. Once we have these pieces of DNA in a tube, we can sequence them and establish the order of the approximately three billion base pairs of human DNA.

An example of the use of positional cloning is the search for the gene for choroideremia. Mapping the gene for a disease like choroideremia, a rare X-linked disorder, is fairly straightforward because we can deduce from the family pedigree that the disease is X-linked and, therefore, we have automatically narrowed the search to the X chromosome. We then select DNA markers from different regions of the X chromosome and follow the transmission of these markers through a family where choroideremia is present. Markers that are passed on in association with the disease are those closest to the choroideremia gene itself . Therefore, the location of the marker points to the approximate location of the disease gene on the X chromosome and the gene itself can be sought in this area. Using this approach, the gene for choroideremia was successfully cloned in 1990[1].

The first three disease-causing genes that were discovered by positional cloning were isolated in 1986 and since then the list continues to grow at an ever-increasing rate. However, I would like to stress the point that these disorders are all basically due to single gene defects. One mutation in one gene, when inherited either in an autosomal recessive, autosomal dominant, or X-linked manner, causes the disease. It has become almost routine now to be able to use positional cloning to identify disease genes that are caused by single defects.

However, let's consider the situation with more complicated types of disorders. If there is a male index case with ischemic heart disease, a male first-degree relative has one chance in twelve, or an approximately five-fold increased risk of also developing ischemic heart disease. If a female is the index case, then a male first-degree relative has one chance in ten, or about six and a half times higher than the general population rate. With a female index case the risk is seven times higher for a female first-degree relative. What we have found here, as the result of careful epidemiological studies, is a familial tendency towards a particular disorder. But these are not the risk factors associated with a straightforward, single-gene, Mendelian pattern of inheritance. The risk figures that we quote are a summation over many, many families, some of whom undoubtedly have single gene defects. Others probably have multiple interacting genes that are involved with environmental components.

How do we dissect out what the genetic contributions are when we find a familial tendency to a serious disease such as early onset ischemic heart disease? What are the challenges that are posed by a so-called

non-Mendelian trait? Genes are involved in some way, but you cannot look at the pedigree the way you can with a choroideremia pedigree and deduce a straightforward pattern of inheritance. There are many complicating factors. Number one is incomplete penetrance. With choroideremia the disease is present by age ten or fifteen, so if you just wait until adolescence to examine a child for the presence of disease, you will definitely see disease symptoms if the child has the defective gene. But in many of the adult-onset, non-Mendelian disorders that involve multiple genes interacting with the environment, there may be incomplete penetrance. This means that it is not always possible to check for the presence of a defective gene by examining the person. That individual may actually have the gene but be symptomless due to incomplete penetrance.

Locus heterogeneity is another major problem in trying to dissect out the genetic contribution to disease. You may have many families with a particular disease, some of whom are affected by mutations at one set of genes, others by mutations involving another set of overlapping or non-overlapping genes. So you have independent loci which makes it very hard to find the signal from any one locus in order to determine a gene responsible for the disease. You could imagine if you had a hundred families in which there was a disease caused by mutations in a hundred different loci, each one different in each family, then if you tried to combine a genetic analysis of all hundred families you would be unable to pinpoint any of those loci because any one of them would be swamped out by the other ninety-nine.

Third, there is the problem of polygenic inheritance; that is, many genes which interact to cause a disease. This makes it difficult to follow the inheritance of DNA markers in individuals who have the disease in their families because there is not just one single region of the genome involved in the development of the disease. An affected individual actually has defective genes in multiple regions in the genome. This makes genetic analysis much harder.

Finally, you can have a combination of problems. For example, many genes may be contributing to the disease and, in addition, there may be incomplete penetrance of one or more of these genes. These factors make studies of this type extremely complex. However, there are important statistical approaches being developed to tackle these problems, and, in particular, there has been a paradigm described and a whole approach delineated called the affected pedigree, or sib pair, analysis. Lambda in particular is the brain child of Neil Risch with contributions by Dan Weeks, Mike Boehuke, Jurg Ott and others. Instead of trying to follow the inheritance of a disease in a family, this approach focuses on affected siblings. Why just affected siblings? First of all, you do not have to worry about lack of penetrance because both are affected. You know that these two individuals, on average, should share half of their genes because of the way they inherited them from their parents. If there is some region of the genome which the affected sibs have in common significantly more frequently than 50/50, that is a red flag indicating that region of the genome may be contributing to the development of this disease.

Now this kind of statistical analysis requires a large amount of data. For example, to detect a genetic locus which increases the frequency of a disease by 50 percent, that is, one which increases an individual's relative risk 1.5 fold, requires 400 affected sib pairs to find a statistically significant difference. Four hundred sib pairs times two people per pair times 300 markers to cover the genome

requires a quarter of a million genotypings using DNA markers. This is a massive undertaking, and five years ago it was science fiction. But not anymore because of the development of the polymerase chain reaction (PCR), which has allowed very rapid genotyping of multiple markers using robotics.

A seminal paper from about a year and a half ago[2] reported the results of a genome-wide search for human Type I or juvenile onset diabetes susceptibility genes using the sib pair analysis just described. The results mean that, in addition to the major diabetes susceptibility locus that we have known about for quite a while (the HLA locus), we now know or suspect that there are multiple other loci including the insulin gene itself and genes in other regions of the genome which play a role in diabetes.

Why do we think that there have to be multiple genes plus the environment involved in Type I diabetes? Because twin studies have long shown that monozygotic twins are not always concordant for juvenile onset diabetes, which means that genetics alone does not produce this disease. Secondly, by examining sibships with diabetes, we know the frequency of diabetes is simply not one chance in four, the way it would be for a Mendelian disorder like cystic fibrosis. So there are multiple genes, and we have now begun to develop the methods to find them.

We can find regions in the genome where a gene might be, but the next step is to find the genes that are in those regions and determine the differences between the genes in individuals who develop juvenile onset diabetes and those that do not. One of the major tools that is going to be very useful is a complete sequence of the human genome because once we have localized the region, then we will be able to find all the genes in that region, get the total sequence of the DNA, and start comparing the DNA sequence of affected individuals and non-affected individuals.

I want to stress that a gene is a complex item. It not only has the pieces which code for proteins, the so-called protein coding regions or exons, it also has a variety of regulatory elements, and there are non-coding regions in between. When we examine genes that predispose to disorders like diabetes or ischemic heart disease, we are, in my judgement, unlikely to find that the defects in the genes are obvious deleterious mutations. They are going to be minor variations in the regulatory regions of genes or in the coding regions of genes . These will be variations which are present in the population and only when interacting with other such variations in other genes and with the environment do they produce some of the serious diseases that we see.

So just knowing that there are five regions of the genome that contribute to juvenile onset diabetes, for example, still leaves the tasks of identifying the genes in those regions and determining how these genes in affected individuals are different from genes in individuals who do not develop juvenile onset diabetes. Additionally, when you find the difference, you need to determine whether that difference is just normal variation that we see in the population anyway or whether is it the functionally important difference that leads to diabetes. These are major challenges that we do not have an answer to yet.

Finally, I would like to stress a couple of other points. One is that the human genome project is going to provide tremendous tools for gene discovery, as I have described to you. It has already made

positional cloning, which was started before the human genome project on an *ad hoc* basis lab by lab, an almost routine approach for single gene defects. Once we find these genes, we can think of three important spinoffs. One is DNA diagnosis; that is, being able to detect abnormalities in genes in individuals. As I have stressed, the more subtle these defects are the more difficult it is going to be to determine what is a defect and what is a variation, which is the molecular version of asking what is a disease and what is a common trait. This is a crucial question that we are going to have to face frequently as we learn more and more about our DNA.

Secondly, with DNA diagnosis we have the option of what is called preventive medicine. This can run the gamut from prenatal diagnosis to carrier screening to detection of predispositions, followed by advising people who are predisposed that they have an increased risk of developing a particular disease, but if they manipulate their environment in a certain way (diet, avoiding exposure, increasing vitamin intake, etc.) they can blunt the predisposition which is present in their genes. This brings up the issue of directive counseling. As an internist I have never had any problem with directive counseling with my patients who were engaging in self-destructive behavior. I do not call in the police when someone insists on smoking, but I certainly do not sit there and tell them it is their choice. Smoking is a problem and needs to be dealt with as a problem in a thoughtful and respectful way. Preventive medicine then flows from this.

Additionally, once we know what a gene defect is, we want to develop gene therapy or designer drug therapy. This is certainly beginning but our ability to diagnose and counsel is skipping way ahead of our ability to intervene therapeutically. That is the nature of the beast but it means that we are faced with a situation of being able to detect a problem without being able to do as much about it as we would like, and that is an enormous challenge to medical genetics.

It is also interesting that ELSI, the ethical, legal, and social issues branch of the human genome center, has identified three major concerns associated with the project: the ethical, legal, and educational ramifications. The diagnostic arm of the human genome project is developing rapidly and it is the arm that is giving people the most trouble and the most challenge in dealing with issues of privacy of information, education, and all of the other ethical, legal, and social concerns.

I have attempted to review where things have been, where they are now, where they are going, and what the particular challenge is to providing genetic services to the population. We are going to be expanding our ability to find predispositions to disease in adults as well as in children and pregnant women. This progress is going to give us new tools, new powers, new responsibilities, and new headaches.

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